History of Neurology in the Netherlands

5702 History of Neurology 05-09-2002 15:25 Pagina 3

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Contents

Preface

Although a few papers and a small book (Schulte and Endtz 1977) have been published on the subject, a comprehensive history of neurology in the Netherlands is still lacking. Schulte and Endtz published their book on the occasion of the International Congress of Neurology in Amsterdam (1977). Following their untimely death, I decided to start a 'history section' within the Netherlands Society of Neurology in order to continue as well as enlarge upon their work. Scientific meetings have been held every year and at each meeting one of the Dutch neuroscientists of the past figured among the subjects presented. One of the objectives of the history section included the realisation of a comprehensive book on the history of neurology in the Netherlands.

In anticipation of the centenary anniversary of the Netherlands Society of Neurology in the 1990s, the board of the Netherlands Society of Neurology commissioned its history section to compose a centenary book. The history section had originally planned to put together a book as described above; the board, however, preferred a book on eponyms. This publication (Koehler, Bruyn and Arts [eds.] 1995) was well appreciated and a modified form, (Koehler, Bruyn and Pearce [eds.] 2000) met with unreserved acclaim. Despite all this, the board of the history section persisted in its wish to realise a book on the history of neurology in the Netherlands and requested the members Frederiks, Bruyn and Eling to be the editors.

The boards of the history section and of the Society itself welcome the present product. It not only provides biographies of some eminent Dutch neuroscientists but also approaches the subject from several perspectives, including the significance of the affiliated non-academic centres, which, alongside the academic centres, played a substantial role in Dutch neurology throughout the 20th century. It also describes the evolution of neurosurgery, initiated by the efforts of Brouwer, the first professor of neurology, who recognised its importance in the 1920s. Furthermore, the evolution of subspecialties and training in neurology are presented. As well as to the editors, the Board of the Netherlands Society of Neurology wishes to express its gratitude to all authors who contributed chapters. The book will become an important source for the Dutch as well as for colleagues abroad who wish to read about the history of Dutch neurology, and hopefully also for those who wish to do further research on this subject as there are many aspects that still need further elucidation. As for the Society, making plans for the future will be more successful if it is done on the basis of a solid knowledge of its history.

Dr. P.J. Koehler,
President of the Netherlands Society of Neurology,
Utrecht, April 2002

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Editorial Account

A number of sessions and consultations to decide on the form and contents led to an editorial consensus on the concept and format of the book now offered to the reader's critical eye. He will note that the structure basically consists of a series of formal aspects of neurology's development in our country since the *fin de siècle*, followed by a series of biographical portraits of some of the neurological coryphaei who dominated the Dutch scene in the past.

We are aware of lacunae, blemishes and shortcomings that are as unwished for as they proved inevitable. Most of the authors are medical men; none of them, perhaps with one exception, are professional historians. A good deal of study of the minutes of meetings of various *gremia* (such as neurological societies and institutes, university council meetings, governmental or municipal committees, in short, archival research of sources) would have been (and ever will be) requisite for an in-depth presentation of most chapter topics. An example is the chapter about Wertheim Salomonson, which shows that even Winkler's 'memories' are not impeccable. A strive for the desirable amount of source research was incompatible with the publisher's time schedule, moreover, the book's appearance is six years serotine (the centenary of the Netherlands Society of Neurology having taken place in 1996) for which we can only offer a choice of apologies, ranging from the septa- to octagenarian age of quite a few authors, to our national characteristic of acting with alacrity, to wasting time in frustrated, amateurish attempts at archival work, to the protracted wait for the submission of manuscripts by some authors.

The series of special topics is somewhat of a hybrid: why add two categories of neurological disorders to a sequence of specialities and subspecialities? And, while you are at it, why not include multiple sclerosis, or migraine, or cerebrovascular disease? Of all imaginable excuses varying in validity or credibility, such as 'we found no author willing, ready and able to write it' or 'sheer arbitrariness', the best we can offer is the time, the size and consequently the cost of the book.

We selected 15 neurologists to be portrayed. We started with 38. The two decisive selection criteria ('no longer in the land of the living'; 'of international repute') meant that, with bleeding hearts, we had to eliminate many. Not quite all though, and the final list might well have included just over 20, which we would have wished. So be it: history is not always just. We can only console ourselves (and, hopefully, the reader) by the consideration that, if it is true that the greatness of a man can only be measured by the length of time he was able to frustrate the progress of science, we saved at least some Dutch neurologists from such *odium* by omission.

The reader will undoubtedly notice the predominance of chapters with a neuroanatomical slant. That is no accident. Between 1880 and 1930 the foundations that were laid for neurology were the normal and pathological components of the domain. After World War II neurophysiology in our country offered nothing to arouse attention internationally, and neurochemistry remained all but imaginary. Is the solid Dutch mind by nature inclined to choose form over function? The selection certainly did not result from editorial prejudice.

We acknowledge our grateful indebtedness to the authors of the chapters, knowing from personal experience how much time, energy, and even expense they invested to meet their commitment. Without them, this book would not have become reality. In particular, we honour the memory of Professor Hans Lakke, who served so admirably for many years as chairman of our Section of the History of Neurosciences.

Which leaves us with the sad duty to pay tribute to the memory of a dear friend and neurologist, Dr David Moffie, who passed away last November 16, 2001 at the age of 86. An old-fashioned neurologist who knew neuroanatomy and neuropathology in detail, gentile yet gallant David survived the Nazi camps, losing his wife in the gaschambers, built a practice after the war in Amsterdam, gained undisputed prominence among colleagues, remained active in the Netherlands Society of Neurology, wrote a multitude of neurological papers, and died a few weeks after having finished the chapter on Bolk in the present book.

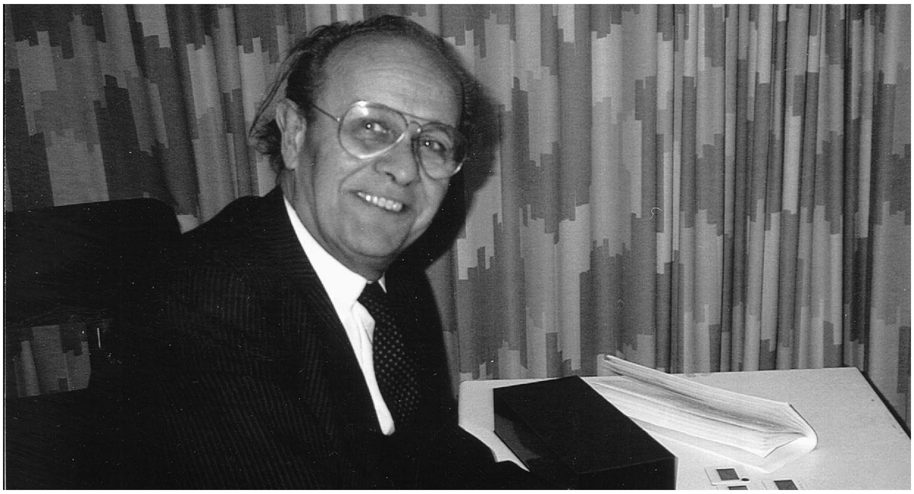
The editors now take their leave, wishing the book well on its journey to various destinations, in the hope that the readers may derive as much pleasure from digesting it as the editors had in shaping it.

April 2002

J.A.M.F.
G.W.B.
P.A.T.M.E.

In memoriam Professor Dr George W. Bruyn

14th December 1928 - 23rd June 2002



Having completed the four-year process of editing this book, the sad news reached us of the sudden and untimely death of our dear friend and highly esteemed co-editor Professor George W. Bruyn.

George Bruyn died in a year in which he not only finished his contribution to the present book as editor and as author of several chapters, he also published several papers on neurological and historical topics, another book, *The Nobel Prize in Medicine*, and, last but not least, with volume 78, he completed this year his *magnum opus*, the *Handbook of Clinical Neurology*. It was a very busy year for him indeed.

The present book could never have been achieved without the inspired, careful and expert help of George Bruyn.

George Bruyn was professor and chairman of the Department of Neurology at Leiden University from 1975 to 1992. He was editor-in-chief of three journals: *Excerpta Medica*, *Journal of the Neurological Sciences* and *Clinical Neurology and Neurosurgery*. In the same period he published some 450 papers. In international neurological circles George Bruyn is known as a gifted and erudite neurologist. In the Netherlands he was one of the last giants in clinical neurology.

My own friendship with George Bruyn started in Amsterdam in the 1950s when I contributed to *Excerpta Medica* and the *Handbook of Clinical Neurology*. He was always an open-minded and very helpful friend, and it was always a joy to work with him.

Many colleagues will miss his valuable critical advice, his friendship and his humour. He will be remembered for his brilliantly spirited and flamboyant presence. And we will remember him always with respect and warmth. We salute his memory.

Jos Frederiks

The Development of Neurology in the Netherlands

1

A bird's-eye view

G.W. Bruyn and P.J. Koehler

The reader may well ask, on seeing the title of this chapter, whether clinical neurology, short and simple, is going to be surveyed or whether the primary, basic provinces of neurology, such as its anatomy, physiology and pathology will also be addressed.

Such questions characterise the modern neurologist; they would never have arisen in the minds of our predecessors, the late 19th to early 20th century neurologists. The latter did not distinguish at all, or at best only marginally, between basic and clinical neurological domains; indeed, they also felt quite at home with psychiatry, the very matrix from which neurology originated in the Low Countries. Psychiatry was considered a special sort of neurology from ± 1870 to ± 1920, a point of view held by such coryphaei as Griesinger, Meynert, von Monakow, Edinger, Wernicke, Spielmeyer, Pick and von Gudden.

'Biological' psychiatry is not a new fad, invented in the 1970s, against which pseudo-progressive Don Quixotes waged war. It has already existed for a century and will, if modern neuroscience continues to advance at the same pace as it has done over recent decades, be the ultimate victor in a conflict as contrived as it is trivial. Therefore, the dilemma posed above, is essentially a fatuous one for a historical survey. Our predecessors felt no antithesis between basic and clinical neurology and none between neurology and psychiatry. Were the two last-named not both domains of deranged nervous system function? And, in consequence, was it not the exclusive province of the qualified neuropsychiatric specialist to diagnose (dia-gnosis = passed through knowledge) and treat? It certainly was not the province of the politically prejudiced agitator.

This view of neurology in its basic and clinical aspects (including psychiatry) as a holistic knowledge domain persisted up to the mid-20th century. For instance, at the International Congress of Neurology in Berne, 1931, von Monakow's successor, M. Minkowski defined neurology as " the science of the structure and all functions of the nervous system, in health and disease, in man and animal, in the foetal, infantile and adult organism" (Minkowski 1931, p.361). Even if he forgot the senile state, and death (a neurodiagnostician's prerogative!), this definition seems quite large, but eminently defendable. About 30 years later, no one less than the astute neuroclinician F.M.R. Walshe, in concordance with Minkowski, defined neurology as the domain that includes "the morphology and physiology of the nervous system, its chemistry and physics, in the normal state as well as in its deviations caused by disease and injury." In short, neurology is the natural domicile that lodges *all* neurosciences.

Many, if not the majority of the mental hospitals in the Netherlands used to have a laboratory for anatomy or pathology where the psychiatrists felt at home and where many *pur sang* neurologists-to-be started out. In the Deventer asylum 'Brinkgreve', the psychiatrist W.H. Cox invented the improvement of the Golgi-stain that rendered him eponymous immortality (Golgi-Cox). Jelgersma, neuroanatomist at heart, began his career in the mental hospital 'Meerenberg', just like the neurologist C.T. van Valkenburg upon his return from Zurich. The neurophysiologist J.G. Dusser de Barenne, in his tender years, started out as a psychiatrist in the Meerenberg asylum and spent much of his time in its laboratory. The neuropathologist F.C. Stam at the Vrije Universiteit assumed the chair of psychiatry there, but is better known for his work on leukodystrophies and his *princeps* observation of 'grape-bunch'-dementia (much later interpreted as polyglucosan-body dementia). Similarly, V.W.D. Schenk, psychiatrist at the 'Poortugaal' mental hospital earned respect for his prolific output of thorough neuropathological papers rather than for his scarce psychiatric papers.

Alongside the psychiatric institutes, (almost) all university Departments of Neurology had their own neuropathological laboratories, their own neuropathologist as well as their own CSF-lab up to the late 1980s; residents' training curriculum included a three-to four-month stay there. These are things of the past. In an era when millions of people drive an automobile without having the foggiest notion of the difference between a two-or four-stroke engine, or how a transmission works, or why there are pinion wheels in the axle's differential, neurologists can practice unaware of the location and function of the nucleus accumbens, or Luys' body, or the V1 to V5 compartments of the occipital striate cortex.

Considering these aspects of neurology's past, the present survey should attempt to comply with the definitions proposed by Minkowski and Walshe. Though they are a mirage today, once upon a time they were reality.

This survey, being restricted to the period 1890-2000, will not provide an exposition of Dutch neurological studies or activities in earlier times. These have been briefly mentioned in the survey by Koehler, Bruyn and Moffie (1998) and are left to potentially prospective authors for an in-depth source research and synthesis, interesting as such a study of 'prehistoric' Dutch neurology in which the 'nerve-force', etc., of vitalism was rampant, may be.

Neither will the present chapter attempt to place 'Dutch' neurology in the frame of European (English, French, German) neurology. With the exception of a few neuroscientists, the picture that would emerge from such a comparison possibly might not overly impress the Dutch reader even if one allows for the proverbial aplasia of the cortical centre of chauvinism among the Dutch. The reasons for the less than exuberant role Dutch neurology played on the European scene are manifold. First, there is the language barrier: hardly a soul beyond the Dutch borders could read the *Psychiatrische en Neurologische Bladen*, so that papers published in that home-journal remained lost to the outside world. Whereas papers and monographs published in England, France or Germany enjoyed a much wider readership if only because of their much larger populations, and because the traditional Dutch familiarity with foreign languages gave its neurological *litterati* ready access to foreign publications, neurology in our country could be compared to a semi-permeable membrane: everything could get in, but next to nothing could get out. Secondly, the Dutch national attitude was (and still is) more inclined to promote mercantile, moral-pastoral and practical issues than scientific research, so that budgeting for scientific research long remained non-existent or at best stingy. Add to this the factor that medical education, unlike the tradition elsewhere, emphasised theory rather than experiment or exploration, plus a consensus that proper patient care should override any other priority, all this combined with a fair measure of self-contentedness if not cosy smugness, and the reader may be filled with compassionate understanding for the modesty of our public presence *in foro neurologiae mundi*.

Without going into detail about the teaching vicissitudes of Delprat in Amsterdam or J.P.T. van der Lith in Utrecht (most of us know the accounts by Donders in 1884 and Winkler in 1930 on the introduction of tuition in psychiatry and neurology at university level), it would be unfair, however, to lay the blame for the unfortunate initial state of affairs alluded to above exclusively at the doorstep of the Dutch government or its administrative bodies. The universities themselves, including their Faculty of Medicine Councils, should be held equally accountable. In retrospect, it seems that all too often an atmosphere of intrigue, political infighting caused by pressure groups, self-interest or religious prejudice, or even sheer stupidity, prevailed in those lofty *gremia*. For example, the Provincial States of Groningen requested the university to instigate a chair for Psychiatry, but this request was rejected under the pretence that wards for psychiatric patients were neither desirable nor tolerable in the new University Hospital that was on the verge of being built. A few other examples may delight and convince the reader.

Leiden's Faculty of Medicine continued to bathe in the past glory of Boerhaave, van Swieten, de le Boë Sylvius, Gaubius, etc., and remained impervious to the signals of changes in the fields of chemistry, physics, physiology and anatomy that threatened its traditional teaching. Leiden succeeded in keeping the howling dogs of progress outside its bastion, until the (neuro-) physiologist van Deen fled the narrow-minded atmosphere for an Ordinariate in Physiology in Groningen (1851) and modern teaching obtained its first chance in the faculty with the appointment of the physiologist A. Heinsius, a former pupil of Donders and Schroeder van der Kolk. Like van Deen, Jacob Moleschott had been a collaborator of Donders, but because of his anti-vitalist and materialistic *Weltanschauung* ("Ohne Phosphor keine Gedanken") stood no chance of a professorate in predominantly Calvinistic Academia. Instead he accepted a series of invitations to assume a chair abroad (Heidelberg, Zurich, Turin and Rome), gained international fame, ultimately winding up as Senator in Rome after he had shed the shackles of his original nationality.

An example of rules persisting from that period, something that is unimaginable today, is the *Limburg Act* of 1917 (legislator Joseph Limburg, 1866-1931). This act allowed, for the first time in our country, pupils from the HBS (i.e., Higher Burgher School) who had had no solid education in the Greek and Latin languages – in contrast to pupils of the Gymnasiums – to take examinations and defend a thesis at the universities' faculties of medicine, an act that enabled our comparative neuroanatomist of international repute, Ariëns Kappers, to have his thesis accepted as recently as 1922 and earned him a mere Extraordinariate as late as 1929. Of course, despite the *Limburg Act*, university study of the humaniora, i.e., the study of philosophy, law, literature, theology, archaeology, etc., remained closed to those who had not attended a Gymnasium.

Another symptom of the atmosphere at the time is the fact that G.E. Voorhelm Schneevoogt (1814-1871), Extraordinarius Psychiatry and Neurology at Amsterdam with lodgings in the Buitengasthuis (the later Pavilion III of the Wilhelmina Gasthuis) where he worked and lectured, was sacked by that Hospital's Regents the moment he married in 1861, as rules excluded the holy state of matrimony for resident staff-physicians. This event terminated tuition in both disciplines. That rule apparently exerted its 'validity' still 50 years later, as we found a confirmation of it, by chance, in a letter dated 8 July 1906 which van Valkenburg wrote to von Monakow, conveying the good news that he, van Valkenburg, had obtained the position of psychiatric physician at the Meerenberg mental hospital, having been selected from many candidates. Van Valkenburg had applied because: "the position was also suitable for married persons." The senior author of the present chapter recalls, in this context, that, while being resident in neurology in the mid-1950s, the chairman, Prof. Sillevis Smitt, voiced his discontent about the number of married neurologists on his staff. He stated that in the good old days the specialist-to-be-consultant used, by unwritten law, to be available for duty 24 hours per day, to devote all his time to the profession, and, accordingly, not be distracted by other aspects of life. The Netherlands Society of Medicine, backed by the Leiden internal medical man Cohen, rejected an official report from Winkler, Jelgersma and van Tellegen (1891), in which a strongly argued plea was made for the inclusion of psychiatry in the curriculum of medical students, on the grounds that such would overload the students' programme; an unequivocal case of the protection of self-interest, shallowly masked by a *gremium* that meddled outside its province.

Under the impact of the work by, for example, Darwin, Virchow, Pasteur, to mention only a few, the resistance against the modernisation of medicine gave way, as the minds of the younger generation of physicians demanded this. A revolution in neuroanatomy had been produced by the wide-scale introduction of the microscope. Advanced technological instrumentation, such as electrical recording and stimulation devices, made findings possible that revolutionised neurophysiology. International Congresses at which leading issues elicited intensive debates acquired progressive frequency.

Present-day neurologists who love their specialty and can afford the leisure-time to acquire sound knowledge of their speciality's roots in the second half of the 19th century, are advised to read Llewellyn Barker's superb monograph (1903), William Locy's integrative survey or, to whet their appetite, Winkler's lucid survey that is structured like Barker's (1921), or van Valkenburg's succinct paper (1950).

Neurology's advance in these times reflected the overall progress of science, not the least because the second half of the 19th century witnessed a preoccupation with the descent of Man (Cuvier's theory and the Lamarck-Darwin doctrine), the degeneration of Man (Morel-Magnan's concepts) and its related aspects of craniometrics as the yardstick to distinguish between 'lower' and 'higher' races as well as the 'born criminal' (Lombroso). All this was enhanced by the palaeontological finds of the Homo Neandertal-ensis (1856) – whose skull Virchow erroneously interpreted to be one of an idiot –, the much younger Cro Magnon Man (1868) – studied by Broca and de Quatrefages –, and the discovery of an apparent missing link, the skull of a *praehominid* (1891), by the Dutch physician/anatomist/palaeontologist/geologist Eugene Dubois from Amsterdam. He had given up his position of senior lecturer in 1887 to search for fossils in the Dutch East Indies and had entered military service to get there, and saw his adventure crowned with success in Java's Madiun region near the Solo river. The skull, which he interpreted as a remnant of Pithecanthropus erectus or Java-Man, was on exhibition at the 3rd International Congress of Zoology (Amsterdam 1895) and the World Fair (Paris 1901). One can imagine that such an event aroused the academic and governmental circles of a small nation from conservative slumber.

Chairs for Psychiatry were instituted at the four universities; chairs that included (or did not, or only partly so) neurology or 'neuropathology' and often showed periods of vacancy. The process can be summarised as follows:

– Amsterdam (after Voorhelm Schneevoogt's amputated tenure 1851-1861): Winkler for Psychiatry and Neurology 1896-1916, with Wertheim Salomonson for Neurology, Electrotherapy and Radiology 1899-1922;
– Amsterdam Vrije Universiteit: L. Bouman for Theoretical Biology, Psychiatry and Neurology 1907;
– Utrecht (after Schroeder van der Kolk, who had the chair of Medicine, Physiology and Anatomy, but lectured regularly in psychiatry prior to 1867, and J.P.T. van der Lith who had been appointed as 'unpaid Extraordinarius in Psychiatry' 1867-1878): Winkler for Psychiatry and Neurology 1893-1896 and 1916-1925, with interregnums by Ziehen 1900-1903 and Heilbronner 1904-1914;
– Groningen: Wiersma for Psychiatry 1903-1929, including Neurology from 1912 onwards, followed by van der Scheer for both disciplines 1930-1949;
– Leiden: Jelgersma for Psychiatry 1899-1930, with lectorates for Neurology (Ernst de Vries 1913-1925 and A. Gans 1929-1945); in 1946 Rademaker, who was Professor of Physiology there, was also charged to chair Neurology.

At last, some structure was being achieved, albeit that the dominant foundation and architecture continued to bear the seal of the authorities' preoccupation with the care of the insane. The high-quality neuro-(patho)-anatomical and neuroclinical work of the initial protagonists and their pupils was tolerated, then accepted, and, much later, officialized.

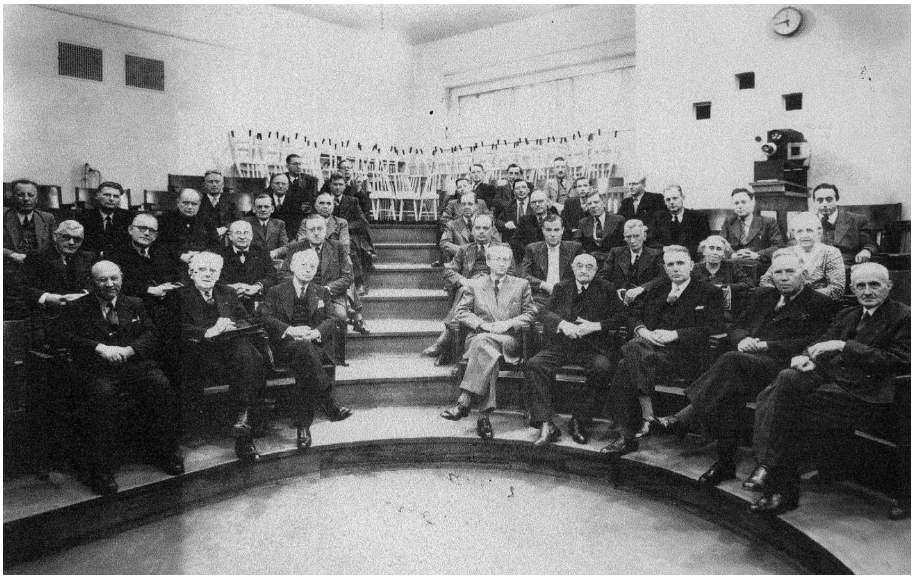


Figure 1.
Meeting of 'Society of Amsterdam Neurologists', October 1949 (40-year anniversary) in 'ouden collegezaal' [old auditorium], Pavillion III, Wilhelmina Gasthuis, Amsterdam.
From left to right, front row: Koster, Brouwer, Van Valkenburg, Van der Horst, Coenen, Tammenoms Bakker, unknown, unknown.
Second row: Stenvers, Biemond, Van der Scheer, unknown, Van der Lugt, Lorentz de Haas, Ernst de Vries, De Lange, Mackenzie-Van der Noorden.
Third row: unknown, Sillevis Smitt, Hocken, Verhaart, De Vet, Posthumus Meyjes Sr., unknown, unknown.
Fourth row: Verjaal, unknown, Tans, unknown, Droogleever Fortuyn, five persons unknown, Lenshoek, Moffie, unknown, Grewel.

After this period of gestation, the neuro-neonate in a psychiatric cradle showed an unexpected growth spurt. If the birth had been initiated by a complex of factors, such as the concentration of neurological forces (1896) within the Netherlands Society of Psychiatry (1871) and the creation of Chairs by the appropriate authorities in addition to the modernisation forces sketched above, another complex of factors induced the growth spurt. Some of them might be identified: the International Congress of Psychiatry, Neurology, and care for the Insane at Amsterdam in 1907, the establishment of the Central Institute for Brain Research at Amsterdam (1909), the creation of the Society of Amsterdam Neurologists (1909), and that of the International League against Epilepsy (1909) by J. Donath (Hungary), A. Marie (France), and L.J.J. Muskens and J. van Deventer, both in Amsterdam.

Over 800 psychiatrists and neuropsychiatrists from 22 countries attended the 1907 International Congress, in the Concertgebouw. One of the main themes dealt with aphasia and the localisation of speech. The controversy between the 'localisers'

Liepmann and Heilbronner and the 'non-localiser' von Monakow made for a riveting performance, which somehow recalled the debates on the same subject at the 1878 Congress of Medicine in Norwich and the 1882 Congress in London (Goltz vs. Ferrier!), the localizers there apparently carrying away the prize. The discussions between Dutch neurologists and their German colleagues, such as Vogt, Pick, and Binswanger strengthened the resolve of the former to intensify their work, and it was decided that future congresses should not combine the two disciplines, the more so inasmuch as the organising body was left with a substantial financial deficit, as appears from the account of Muskens and Bouman (1908).

A more or less direct result of this congress was the founding of the Society of Amsterdam Neurologists by van London, van Valkenburg, Ariëns Kappers, Winkler, Wertheim, de Vries, Muskens and K.H. Bouman (1909) to concert the energies of *pur sang* neurologists.

In this context, the creation of the Central Institute for Brain Research (1909) proved to be of inestimable influence. Wilhelm His Sr., pupil of Remak and initiator of the *Nomina Anatomica*, had persuaded the Königliche Sächsische Gesellschaft der Wissenschaften to address the 1901 meeting of the International Association of Academies (Paris) with a plea to create a global League of Institutes for research of the nervous system. This led to the formation of the, then famous, 'Brain Commission', which succeeded in getting seven institutes of such signature that already existed together for a communal programme of nomenclature, collection of tissue-material, distribution of research projects among them, etc. (the seven being Frankfurt, Leipzig, Madrid, Philadelphia, St. Petersburg, Vienna and Zürich). Other countries were invited to join. Thanks to the efforts and the official report by Winkler and Bolk, the Netherlands was the first invitee to be able to respond affirmatively, as its Academy of Sciences, the Amsterdam Municipality and University, and the government voted to defray the requisite expenses. The Institute's building, annex to the Anatomy Laboratory, was officially opened on June 8th 1909, at the occasion of which Waldeyer expressed his admiration. Ariëns Kappers became its director, van Valkenburg vice-director and Ernst de Vries assistant. There, Ariëns was enabled to formulate the principle of neurobiotaxis, which rendered him international fame, and he composed the three-volume work on comparative neuroanatomy that remained a hallmark in the field for half a century. The Institute provided the facilities for Muskens' anatomical research on the supravestibular system, the groundwork for de Vries' life-long studies on the glia and, much later, the microglia in post-vaccinial encephalitis (which revealed a relationship with two different durations of incubation-period), as well as the basis for Bolk's perceptive foetalisation theory in human ontogeny.

The establishment of the International League against Epilepsy in the same year produced a major impetus for the organisation and treatment of epileptics in our country, an improvement to which the names of Muskens, van Deventer, van Valkenburg, Lorentz de Haas, Ledeboer and Meinardi are closely tied.

All that, plus the upheaval of World War I, constituted decisive factors in changing the approach and activity in neurology. Between 1918 and 1929, an avalanche of

Dutch textbooks and monographs on the anatomy, physiology and disease of the (central) nervous system appeared on the market. The awareness of neurology as a specialism in its own right spread. The creation of chairs in 1923 (Amsterdam) and 1936 (Utrecht) bears witness to this. Among neurological papers, neuroanatomical and neuropathological observations rather than exclusively clinically orientated reports figured prominently in the issues of the *Psychiatrische en Neurologische Bladen* of those early years. For these, the reader is referred to the chapter on 'Publications'.

In spite of that, the number of practising specialists limiting themselves to deal with neurological disorders *senso stricto* remained modest, if only because formalised residency-training continued to include both psychiatry and neurology. Medical training followed the traditional pattern of five years of theory preceding two years of rotating internships, which elicited Sir Frederick Mott's comment, while dining at Winkler's home in the mid-thirties, "you teach the students knowledge, we teach them practical science."

As a result, activity in practice remained (as of course it should) focused on proper diagnosis and treatment; any supervening research depended largely on the preferences and idiosyncrasies of the individual neurologist. Papers submitted to the home journal consequently remained largely anecdotal, without experimental or statistical background. In addition, the home journal continued to be a hybrid because it published a major portion of psychiatric papers. In this period between the 1930s and the 1950s, the university neurological departments did not strike a much better figure though, as far as research is concerned. Efforts focused on sound bedside teaching, under the umbrella of up-to-date knowledge. Apart from a smooth discharge of clinical duties, there was scarcely a concerted effort by staff to deal with one or two foci of research. If the latter was done at all, the work issued by these academic departments in those years can be characterised as haphazard, non-systematic and unorganised, without a central theme, and manifesting usually in the form of MD theses and coincidental observations, without inherent consistency. *Grosso modo*, the work from this period betrays an individualistic tendency, or solipsism, and a scotoma for the teamwork that American colleagues are so renown for.

In order not to convey the idea of a disparaging sketch of the overall performance during that period, one may do well to mention the work of a few individuals, without any attempt at completeness. Jelgersma reported the *princeps* observation of striatal cell depletion in Huntington's chorea; Magnus and de Kleijn will stand out forever for their work on neck and labyrinthine reflexes, as will Rademaker for his work on the red nucleus and stance; Droogleever Fortuyn discovered the 3 p.s. spike-wave phenomenon; Biemond identified five or six disease entities that bear his name eponymously; Stenvers elaborated an ingenious way for localising hemispheric lesions involving the callosal fibres by devising the method of 'localisation on imagination' and invented the roentgenological projection ('Stenvers projection') for detecting acoustic nerve tumours at an early stage; Brouwer reported the *princeps* observation of paraneoplastic cerebellar cortex atrophy; Verhaart was the first to identify 'multiple system atrophy'; Ter Braak founded the distinction between two types of optokinetic nystagmus, one via a cortical and one via a subcortical pathway; and J.G.Y. de Jong wrote the *princeps* observation of hereditary pressure neuropathies and myotonia laevior. Extending this listing to cover recent decades as well, van Crevel detected the time-related parameters of demyelination; Bethlem the myopathy that became eponymously associated with his name; Bruyn and Kok identified hyperekplexia and with Went defined the mitochondrial disease entity of dystonic Leber optic atrophy; Höweler proved the traditional geneticists' exegesis of the phenomenon of anticipation to be false by demonstrating the causative effect of the number of triplet-repeats; Schouwink initiated the zinc-sulphate treatment of Wilson's disease as did Vermeulen with the immunoglobulin administration in Guillain-Barré's syndrome; Padberg alerted us to the link between Lhermitte-Duclos and Cowden diseases; Kremer revealed the involvement of the lateral nucleus tuberis in Huntington's chorea; Gabreëls' team elucidated a number of mitochondral neuromyopathies; Barth clarified the (congenital) cerebellar-cerebral hypoplasias; and the Ferrari-Frantz team identified the genetic defect in familial hemiplegic migraine. This enumeration indubitably fails to mention quite a few deserving colleagues, but the above came readily to mind and we extend our apologies for any omission.

With the introduction of new techniques of examination ranging from EEG-/EMG-/ECHO-graphy to PEG, myelography, angiography, and CSF-cytology with immunoelectrophoresis, the level of neuro-diagnostics throughout the country kept pace with advancing fronts abroad. If one adds to that the availability of new drugs and treatment modalities, such as artificial hibernation, stereotaxis, intensive care, L-Dopa, neuroleptics and neuroanaesthetics, the neurological domain widened to the extent that a definitive separation from psychiatry was no longer avoidable (1973/4). The introduction of CT/NMR-scanning techniques as well as the nosological revolution caused by the DNA-techniques made such separation all the more imperative. Residency training had to be prolonged from three, to four, to, at the time of writing, six years; update courses and certification procedures were made mandatory; diagnostic/therapeutic consensus-protocolled practice made its entry, be it at the price of concurrent loss of independent thought, inventiveness or originality, but with the advantage of defensive medicine strategy in litigation procedures that multiplied like rabbits. Paradoxically, the more scientifically founded and efficacious neurology became, the more patients started to sue. What with progressive bureaucratisation and 'technification', the profession lost its old predicate of being *free* and part-time group practices became the rule rather than the exception. Some of the 'old horses' find this deplorable and sad, while recognising the inevitability. In the course of a century, society had changed tremendously: a population of a mere five million with a group of less than 50 neurologists had swelled to one of 16 million subserved by more than 600 neurologists. National healthcare had come to cover mandatorily *circa* three-quarters of the population, small hospitals were closed or merged with larger city hospitals to defray the investments required for advanced diagnostic and therapeutic facilities (without, however, succeeding in keeping the cost of a day's stay in a hospital bed below that of, e.g., a Hilton or Intercontinental hotel room and with less privacy and service), private practice at home became all but extinct, and the number of hours spent in filling out administrative forms or attending a motley of committees assumed astronomical magnitude.

Differences between hospitals with regard to the standard of the neurological service they offer largely disappeared over time as the various factors, rules, regulations, etc., took effect in producing a fairly uniform level of quality of medicine, including neurology. The great majority of specialists regularly consult the Internet- and CD-ROM services to keep abreast with their respective fields of competence, and this is quite apart from the obligatory postgraduate courses and certification procedures.

Research at the various academic neurological departments has become more focused with a grosso modo distribution of topics (see table), though a rigid and completely programmed distribution of research-topics is neither feasible nor desirable for obvious reasons. Teamwork between academic neurology staffs and those of closely related disciplines intensified under the pressure of the newest techniques and as the autonomy of the 'old' neurological departments with their own neuropathology/CSF labs and roentgenological services were abolished. Collaboration between young neurologists and molecular biologists materialised with increasing frequency *a pari passu* the detection of ever more gene defects in (hereditary) neurological disorders that hitherto had been regarded as true disease entities, a process which fundamentally unsettled traditional neurological nosology. At the time of writing, at least seven mutations causing hereditary spastic paraplegia are known (goodbye 'Strümpell-Lorrain's disease'!), at least twelve underlying hereditary spinocerebellar atrophies, not to mention the even greater numbers found to cause familial amyloid neuropathies, HSMN-types and the Prionoses. Within living memory, breakthroughs in medicine have invariably originated in the laboratory and rarely at the bedside. In neurology today, it occurs at such a pace and to such an extent that the practising neuroclinician, faced with ever growing lists of genetic differential diagnoses, may be driven to despairing perplexity, notwithstanding the assistance of the above-mentioned Internet and CD-ROM. The complex field of gene-interaction is already on the horizon as is the *rentrée* of neurochemistry as the study of abnormal gene products on neural cells and tissues. The imminent threat to our specialty is that two categories of 'clinical' neurologists will be trained: one for practice and one exclusively equipped for research.

In the not too distant future the science of neuronal networks – of cognition, volition and emotion – holds the promise of a return of the hand of the clock to where it all began, namely the merging of neurology and psychiatry into unity.

Looking back on a century of neurology in our country, one sees turmoil and quiet. At the present, neurology is in a maelstrom. Though some things could have been done better, others could have been done worse. Because of the extensiveness of our specialty's subject, the nervous system, as well as of the encompassing new techniques mentioned above, our natural territory tends to dissolve, and some parts have gone already.

Table I. Sketch of researchtopics at various neurological university departments since about 1975.

- University of Amsterdam
  - Dementias
  - Neuromuscular diseases including: motor neuron disease
  - Motor neuron disease
  - Movement disorders
  - Stroke
  - Infections of the nervous system
- Vrije Universiteit (Amsterdam)
  - Dementias
  - Demyelinating diseases
  - Movement disorders
  - Neuro-oncology
- Groningen
  - Craniocerebral trauma
  - Demyelinating diseases
  - Movement disorders
  - Myasthenia gravis
  - Stroke
  - Neurodegenerative disease
  - Neuroimmunology
  - Neuromuscular disease
  - Neuro-oncology
  - Neuropsychology
- Leiden
  - Movement disorders
  - Migraine/cluster headache
  - Neurodegenerative diseaeses
  - Neuro-immunology
  - Neuromuscular disease
- Maastricht
  - Craniocerebral trauma
  - Neuromuscular disease
  - Neuro-oncology
  - Stroke
  - Demyelinating diseases
  - Neuro-epidemiology
  - Epilepsy
  - Technology assessment
- Nijmegen
  - Demyelinating diseases
  - Epilepsy
  - Metabolic diseases, in particular mitochondrial disorders
  - Neuromuscular diseases
  - Neurodegenerative diseases
  - Neurogenetic diseases
  - Neuro-oncology
- Rotterdam
  - Neuroimmunology
  - Neuromuscular diseases
  - Neuro-oncology
  - Stroke
- Utrecht
  - Stroke
  - Neuromuscular diseases
  - Neuro-oncology
  - Wilson's disease

The actual and future leading neurologists in our country will have to be alert and resolute to avert further weakening of their 'queen of specialties'.

Vivat, crescat, florat neurologia batavorum.

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Academic Chairs

2

P. Eling and P.J. Koehler

Neurology as an academic discipline in the Netherlands is often considered an offspring from psychiatry. However, internal medicine also played an important part, as acute neurological diseases were often treated by internists. The first departments of electrotherapy originated in the department of internal medicine, e.g., the department at the municipal university of Amsterdam, where subsequently Gerrit Waller, Constant Charles Delprat and Johannes K.A. Wertheim Salomonson, residents of the internist Pieter Klazes Pel, worked at the electro-therapeutic outpatient clinic. Psychiatry as a discipline often included neurology. Chairs of psychiatry were founded in the late 19th century. In some instances the word neurology was added (e.g., Winkler's chair in Utrecht was called psychiatry and neurology) or even preceded the word psychiatry (e.g., Winkler's chair in Amsterdam, 1896, was for neurology and psychiatry; this chair was originally for internal medicine). Neurology did not become an independent academic discipline until Bernardus Brouwer was appointed professor of neurology in Amsterdam in 1923. At some universities it took appreciably longer.

Table I. Founding of the Dutch Universities.

University	Founded	Closed
Leiden	1573	
Franeker	1585	1811
Groningen	1614	
Utrecht	1636	
Harderwijk	1648	1811
Amsterdam: Municipal	1877	
Amsterdam: VU	1880	
Nijmegen	1923	
Tilburg[1]	1927	
Eindhoven[1]	1956	
Rotterdam	1973	
Maastricht	1976	

[1]No medical faculty

Leiden, Groningen and Utrecht were the major university cities. Franeker (established in 1685) and Harderwijk (established in 1600) were closed by Napoleon in

1811/1812 (Lindeboom 1972). The retreat of the French occupational army in 1813 opened a new chapter in Dutch history. This also had implications for the universities. In August 1815, the so-called 'Organiek Besluit' [Organic Resolution] was published, a law concerning the organisation of higher education in the northern provinces (i.e., excluding what is known today as Belgium, which became an independent state in 1839). The universities came under state control. For the medical faculties, the law had specific consequences. Next to medicine, surgery and obstetrics became recognised academic disciplines for which independent doctorate degrees were created. Moreover, the law required the development of a medical curriculum, including clinical teaching in 'academic hospices'.

Thorbecke's Law (1865) was another major factor that determined the organisation of the medical profession. Previously there had been numerous kinds of medical and paramedical professions. The new law dictated that there was to be a single title, that of physician, guaranteeing the unity of the medical profession. A practical state exam was organised for the title of physician. A reorganisation of the medical curriculum was also required, by which surgery and obstetrics became obligatory parts of the curriculum.

Next to universities, some cities had 'Illustre Schools'. For instance, in Amsterdam the 'Athenaeum Illustre' was founded in 1632 and a hospice was opened for teaching purposes in 1669 (Zeeman 1932). When legislation concerning medical education was adapted in 1865 aiming to eliminate medical training trajectories that were not under governmental control, the Athenaeum still fulfilled the minimal requirements for a proper medical education. Due to a decrease in students around the 1860s, the Amsterdam authorities asked the national government to reform the Athenaeum into a university. It was incorporated into the newly established Municipal University in 1877, initially boasting ten professors at the faculty of medicine.

Not entirely satisfied by the state of affairs at the public universities, in particular with respect to theology, the Protestants founded their own university, the Vrije Universiteit in Amsterdam (Roelink 1955). In 1880, five professors began teaching at three faculties – theology, letters, and law – with five students. The Catholics followed this example by establishing a Roman Catholic university in Nijmegen in 1923. In order to deal with the post World War II baby boom, new universities were founded in Tilburg and Rotterdam. In Tilburg, however, there is no medical curriculum. Another university was founded in Maastricht in 1976. A further increase in the number of universities was due to the technical colleges (Delft, Eindhoven and Enschede) being renamed (technical) universities.

Following the French occupation (1800-1815), the situation at the Dutch universities was rather poor. The possibilities for research were practically nihil. Laboratories were usually not much more than rather empty rooms. The government, and consequently also the boards of the universities, did not want to spend much money on new developments. New laboratories were created for physiological research in Utrecht and Leiden in 1865, but this had little impact on the study of the nervous system (Pekelharing 1907).

There was usually a limited number of chairs at the medical faculties. Towards the end of the 19th century, the need was felt to create chairs for specialised areas within medicine, starting with psychiatry. Furthermore, the number of medical students was very limited up to 1900. Lieburg (1992, p. 33) mentioned that approximately 15 students received training in the academic hospital in Utrecht per year and 17 students in Amsterdam. With such small numbers, one can imagine that the university boards were not overly eager to create separate chairs for psychiatry and neurology, although a curriculum filled with other subjects was also a much heard argument against the foundation of new chairs.

Utrecht

Jacobus Schroeder van der Kolk (1797-1862) was very influential. He became professor of physiology and pathology in Utrecht in 1826, but also concerned himself with the improvement of care for psychiatric patients. He became Inspector General of Public Healthcare in 1838, responsible for the supervision of conditions in the Dutch asylums, which necessitated his involvement in the planning for better housing and treatment for patients at non-university-affiliated institutions. In the 1850s, he published a number of papers on the structure and function of the spinal cord and the brainstem as the source of epilepsy (see for a more detailed description, Ten Doesschate 1961, Eling 1998), which appeared to be influential. His handbook of psychiatry, consisting mainly of chapters on neuroanatomy, was published posthumously in 1863.

Franciscus Cornelis Donders (1818-1889), student and successor of Schroeder van der Kolk, also made use of his influence at a political level. He recognised that there was a need for a chair in psychiatry. He suggested to *Cornelis Winkler* (1855-1941) that he become reader of psychiatry, but Winkler declined the offer, fearing that he did not know enough about psychology and philosophy. Moreover, he was more interested in investigating the nervous system. Following a study tour to Austria in 1882, he noticed that psychiatry could be performed on a physiological basis. He explained to Donders that he was now willing to become a reader of psychiatry, a position he obtained in 1885. While teaching psychiatry, his neuroanatomical research predominated. The university board created a chair of psychiatry and neurology in 1893, promising that they would also build a clinic for him. When the board failed to fulfil this promise, Winkler left for Amsterdam.

The chair remained vacant until 1900 when *Theodor Ziehen* (1862-1950) moved from Jena (Germany) to Utrecht, but he left again as soon as 1903 to succeed Hitzig in Halle. *Karl Heilbronner* (1869-1914) took over in 1904. In 1907, the board promised him the clinic that was so important for teaching neurology and psychiatry. The new clinic – also known as 'Building III'– was finally opened in 1912. When Heilbronner died in 1914, the board offered the chair again to Winkler and he returned in 1916. Although his views with respect to the basis of psychiatric symptoms were changing, Winkler firmly held to his original standpoint that psychiatry should be studied from a biological point of view. He was explicitly opposed to psychoanalytical ideas.

Winkler retired in 1925 and was succeeded by *Leendert Bouman* (1869-1936) who had occupied the chair of 'theoretical biology, neurology and psychiatry' at the Vrije Universiteit in Amsterdam since 1907. When Bouman died in 1936 the chair was split in two: *Henricus Rümke* (1893-1967) was appointed professor of psychiatry in 1936 and *Willem Gerrit Sillevis Smitt* (1894-1985) was appointed extraordinary professor of neurology in 1938. In 1947 he became full professor of neurology.

Table II. Professors of Neurology in Utrecht.

Professor	**Chair**	**Period**
C. Winkler	Psychiatry and Neurology	1893-1896
Th. Ziehen	Psychiatry and Neurology	1900-1903
K. Heilbronner	Psychiatry and Neurology	1904-1914
C. Winkler	Psychiatry and Neurology	1916-1925
L. Bouman	Psychiatry and Neurology	1925-1936
W.G. Sillevis Smitt (extraordinary)	Neurology	1938-1947
W.G. Sillevis Smitt	Neurology	1947-1965
A. Kemp	Neurology	1965-1982
J. van Gijn	Neurology	1982-

Leiden

The chair of psychiatry was founded in 1899 (Woltjer 1965, Rooijmans 1998). An attempt to get Winkler to Leiden failed. Instead, *Gerbrandus Jelgersma* (1859-1942) was appointed. A clinic had already been founded in a centuries-old castle called 'Endegeest' near the city of Leiden in 1895, also at the request of the university board. From 1897 it acted as academic psychiatric clinic. Close cooperation between local and national authorities created a good environment for treating psychiatric patients and teaching psychiatry. Psychiatric research in those days consisted of neuroanatomical and neuropathological studies. Jelgersma was an expert in neuroanatomy. He started an atlas of the human brain (1906), which was finished and published in 1931 (Carp 1942). Gradually, however, Jelgersma became interested in a new area, that of patients with nervous diseases such as 'neurasthenia'. In 1897, he published a handbook on functional neuroses. When he became a professor, it was agreed that an additional sanatorium for this category of patients would be built. The sanatorium was opened on the grounds of the 'Rhijngeest' property, close to Endegeest (1903), and approximately 200 patients were treated there per year.

Jelgersma was also interested in psychology, in particular in the work of *Gerard Heymans* (1857-1930), who was working in Groningen (see below). However, in sharp contrast to Heymans, he strongly believed that all functional changes implied structural changes and that functional disorders would be considered organic disorders in due course.

When the burden of clinical and research work became too much, he left the teaching of neurology to *Ernst de Vries* (1883-1976). At the occasion, Jelgersma published a lecture, in which he argued that psychiatry and neurology differed. Psychiatry was not an ordinary medical subject, but required insight into psychology and 'understanding' of a person.

Following his medical studies in Amsterdam, De Vries had written a dissertation on neuroglia (1909) under von Monakow in Zürich. He had acted as superintendent of 'Voorgeest', a youth section of Endegeest since 1911. He was appointed private lecturer of neurology in 1913. De Vries left for China in 1925, and *Abraham Gans* (1885-1971), trained in Amsterdam, took over in 1927. A long period of discussions started about further integration of psychiatry and neurology in the university. The issue of new buildings on the grounds of the academic hospital became a hot item. An independent neurological department was not created within the academic hospital until 1955, although the university had decided to found a chair for neurology before the war. Gans was installed as reader of neurology again in 1945, however, the university authorities did not regard him as the best person for the chair. *Gijsbert Rademaker* (1887-1957), professor of physiology, had already stood in for Gans during a period of absence because of illness, and when Gans resigned in 1946, the university decided to change Rademakers' chair of physiology into one of neurology. He retired in 1957 and was succeeded by *W.J.C. Verhaart* (1904 - 1983), who founded the Leiden Institute of Neurological Sciences, unifying neuroanatomy, neuropathology, neurosurgery and clinical neurology.

Table III. Professors of Neurology in Leiden.

Professor	Chair	Period
G. Jelgersma	Psychiatry and Neurology	1899-1930
A. Gans (Reader)	Neurology	1927-1945
G. Rademaker	Neurology	1946-1957
W.J.C. Verhaart	Neurology	1958-1970
A. Verjaal	Neurology	1972-1975
G.W. Bruyn	Neurology	1975-1992
R.A.C. Roos	Neurology	1993-
A.R. Wintzen (extraordinary)	Neurology	1995-

Amsterdam: Municipal University

The Athenaeum Illustre in Amsterdam was the first place where psychiatry was officially taught (Zeeman 1932). *Gustaaf Eduard Voorhelm Schneevoogt* (1814-1871) had been appointed extraordinary professor of 'neuropathology in connection with the doctrine of insanity' in 1851. It took until 1896 before a chair of psychiatry and neurology was founded. Winkler, in conflict with the university board in Utrecht, acquired both a chair and a clinical ward, pavilion III at the Buitengasthuis. Winkler also acquired a neurological clinic, originally Hertz's internal clinic, at the Binnengasthuis. Here he developed his ideas on the localisation of functions. He attempted to demonstrate that the inner layer of the cortex was organised according to functions whereas he supposed the outer layer to have a more diffuse, integrative character. He also wrote on dermatomes, optical and transcortical aphasia and on many aspects of neurosurgery. WhenWinkler returned to Utrecht in 1916, he was succeeded by *Klaas H. Bouman* (1874-1947), one of his disciples.

Winkler cooperated with *Johannes Wertheim Salomonson* (1864-1922), who worked at the Binnengasthuis and had a special interest in treating neurological patients by electrotherapy. After Konrad Röntgen had discovered the x-ray technique in Würzburg (1895), Wertheim demonstrated the procedure to his colleagues in February 1896, and the first röntgen-picture of a hand was published ten days later in the *Nederlands Tijdschrift voor Geneeskunde*. The significance of this procedure was immediately recognised and Wertheim was given the apparatus to examine patients at the Binnengasthuis. He was offered an extraordinary chair of neurology and electrotherapy in 1899, radiography being added in 1900.

When Wertheim died in 1922, the chair was split into two, one for neurology and one for psychiatry. *Bernard Brouwer* (1881-1949) was appointed to the chair of neurology in 1923, while K. H. Bouman kept the chair of psychiatry. In 1929, a new building was opened in which Brouwer's neurological clinic was housed.

Brouwer, a former pupil of both Winkler and Wertheim, held the chair of neurology for a period of 23 years. These may be regarded as the formative years of neurology; ones in which Brouwer played a dominant role. Many of his disciples obtained chairs once they had been founded at other universities (Schulte and Endtz 1977). Brouwer was one of the few clinical neurologists to be most active in basic research. The central theme of his research was the central representation of the retina in the cortex. When *Cornelius Ubbo Ariëns Kappers* (1877-1946) died, Brouwer was also appointed director of the Central Institute for Brain Research, a position he held until his death. *Arie Biemond* (1902-1973), another central figure in the history of Dutch neurology, succeeded him as professor of neurology. Like Brouwer, he was born and educated in Amsterdam. First he became Brouwer's assistant; later he took over his chair, continuing his line of research. His textbook, *Hersenziekten. Diagnostiek en therapie* (1946) was also published in English (*Brain Diseases*, 1970).

Amsterdam: Vrije Universiteit

Although the Vrije Universiteit, founded in 1880, did not have a medical faculty until 1950, a chair for 'theoretical biology, neurology and psychiatry' was founded by the Association for Christian Care for Mental Patients in the Netherlands in 1907

Table IV. Professors of Neurology in Amsterdam Municipal University.

Professor	Chair	Period
C. Winkler	Psychiatry and neurology	1896-1915
J.K.A. Wertheim Salomonson (extraordinary)	Neurology, electrotherapy and radiography	1900-1922
K.H. Bouman	Psychiatry and neurology; From 1923: Psychiatry	1916 -1919
B. Brouwer	Neurology	1923 - 1946
A. Biemond	Neurology	1947 - 1971
W.A. Den Hartog Jager	Neurology	1971 - 1980
H. van Crevel	Neurology	1980 - 1991
M. Vermeulen	Neurology	1991 -
J. Stam	Neurology	1993 -

(Roelink 1955). Leendert Bouman was appointed and became director of the Valerius clinic for neurology and psychiatry. Bouman was trained in the neuropsychiatric tradition. The association that paid for the chair expected him to defend a more anthropologically oriented psychiatry and these two points of view resulted in a slowly increasing tension. Finally, Bouman left (1925), as did a few of his co-workers. Due to ideological discussions, the chair remained vacant until 1928, when *Lammert van der Horst* (1893-1978) was appointed. He had a broad interest and, among other things, this resulted in the installation of the first electroencephalograph in a Dutch clinic. Like Bouman before him, van der Horst practised at the Valeriuskliniek. A separate neurology unit was established there in 1945. The medical faculty was initiated in 1950, but the section Neurological and Neurosurgical Sciences, with special emphasis on stroke, neuro-immunology, neurotransmitters and neuropsychology, was not founded until 1974.

Table V. Professors of Neurology in Amsterdam Vrije Universiteit.

Professor	Chair	Period
L. Bouman	Theoretical Biology, neurology and psychiatry	1907-1925
L. van der Horst	Psychiatry	1928-1963
F.C. Stam	Neuropathology and Psychiatry	1962-1991
J.F. Folkerts	Neurology	1961-1976
J.H.A. van der Drift	Neurology	1977-1987
J.C. Koetsier	Neurology	1980-1997
J. Heymans	Neurology	1997-

Groningen

In 1876 the provincial authorities asked the university to create an opportunity for teaching theoretical and practical aspects of psychiatry (Teelken, van Weerden and van Zomeren 1991). The medical faculty reacted negatively, not feeling comfortable about the thought of having psychiatric patients in the hospital. In a report, written in 1890, Winkler, Tellegen and Jelgersma pleaded that an academic hospital should have a psychiatric clinic for educational purposes but the faculty maintained its disinclination. In 1896 *Enno Dirk Wiersma* (1858-1940) opened a private clinic with seven beds, and a year later, he was asked to teach psychiatry as a private lecturer. The longstanding discussion between the authorities was settled when a new academic hospital, including a psychiatric unit was opened in 1903. Wiersma was appointed professor of psychiatry in 1903. He had a great interest in psychology and was influenced by Gerardus Heymans, the first professor of psychology in the Netherlands. Wiersma was an adherent of Heymans' 'psychic monism' and believed that all material phenomena were the result of the working of consciousness. Heyman and Wiersma worked closely together and performed experiments on breathing, pulse rate and skin temperature in relation to mental states. They were also interested in developing a theory of personality traits. Neurology was added to Wiersma's task in 1912, and a new psychiatric and neurological clinic was built in 1916. The clinic was overcrowded almost from the beginning, and the situation was very bad for the patients. Wiersma officially remained in office until his 70th birthday but in fact continued for a while after since no successor was yet available. In his valedictory address he again pointed out that psychiatry and neurology should be kept together, if possible, and also emphasized the role of psychology.

Willem Matthias van der Scheer (1881-1957), former assistant of Winkler in Amsterdam, succeeded Wiersma in 1930 (although the latter did everything in his power to prevent it). Van der Scheer was in favour of the combination of psychiatry with neurology, but could not continue Wiersma's line of psychological research. He was much more a clinician than a scientist. He tried to implement the proposals for 'active therapy' (occupational therapy) in his wards. When he retired in 1949, the search for a suitable candidate made it clear that a separation of psychiatry and neurology had become imperative. *J. Droogleever Fortuyn* (1906-1999) became professor of neurology. He regarded the departure of psychiatry from the clinic (in 1969) as well as the developmental neurological unit headed by Prechtl as the great innovations under his regime. He established units for neuropsychology, paediatric neurology and neurochemistry.

In the 1970s, intense discussions about the separation of neurology and psychiatry had repercussions at the neurology department in Groningen. *Jan Minderhoud* (1932-) took over the chair from Droogleever Fortuyn (1974). His collaboration with the neuropsychological unit was extremely fruitful and Groningen became a centre of expertise for brain injury that is recognised worldwide. *Hans Oosterhuis* (1932-) was appointed professor of neurology in 1976 and *Hans Lakke* (1928-2001) in 1987.

Table VI. Professors of Neurology in Groningen.

Professor	Chair	Period
E.D. Wiersma	Psychiatry	1903-1912
E.D. Wiersma	Psychiatry, including neurology	1912-1928
W.M. Van der Scheer	Psychiatry and Neurology	1930-1949
J. Drooglever Fortuyn	Neurology	1950-1974
J. Minderhoud	Neurology	1974-1995
H.J.G.H. Oosterhuis	Neurology	1976-1997
J.P.W.F. Lakke	Neurology	1987-1993
J.H.A. de Keyser	Neurology	1995-

Nijmegen

The Dutch royal family has the protestant faith, and Protestantism dominates in the northern and western provinces of the Netherlands. The Catholics, concentrated in the southern part, were eager to improve their position, politically and socially. This also involved the formation of Catholic schools and a Catholic university. The University of Nijmegen was founded in 1923, but at that time there was no medical faculty. Just before World War II, *J.J.G. Prick* (1909-1978), a pupil of Brouwer, was invited by the board to move from Amsterdam to Nijmegen to help set up such a medical faculty. A small unit for patients with nervous diseases was prepared for him in a local hospital, as a kind of transitional arrangement. In fact, the unit was only used for psychiatric patients (Prick 1975). The war interfered with the realisation of the plans for a medical faculty. Prick was appointed as private lecturer in forensic psychiatry at the faculty of law in 1941. After the war, he became professor of psychology in the faculty of letters and philosophy. The experience of these early years taught Prick the relevance of the behavioural sciences. Following years of discussion about the necessity of a medical faculty in Nijmegen, it was decided that a complete (not just theoretical subjects) medical faculty should be formed. The faculty started in 1951 and Prick was appointed professor of neurology, psychiatry and psychology in 1953. Although at other places, many would agree that the area of neuropsychiatry had become too large to be mastered by one individual, Prick apparently did not experience this as problematic. In fact quite the opposite could be argued. According to his close friend and colleague, the physiologist and psychologist *F. J.J. Buytendijk* (1887-1974), he believed that a good and complete understanding of the functions of the nervous system required a holistic, anthropological approach to the patient. Prick was not in favour of a division of his chair and when it finally happened in 1971, he chose for the one of neurology. In line with this choice (and thanks to his connections at governmental level), a new Institute for Neurology and Neurosurgery was opened in 1973. He was succeeded by *Bento Schulte* in 1980, who is known for his neuroepidemiological and historical studies.

Table VII. Professors of Neurology in Nijmegen.

Professor	Chair	Period
J.J.G. Prick	Psychiatry, Neurology and Psychology	1945-1971
J.J.G. Prick	Neurology	1971-1978
B.P.M. Schulte	Neurology	1980-1991
G.W.A.M. Padberg	Neurology	1994-

Rotterdam

One of the local hospitals in Rotterdam, the Coolsingel Hospital, became the larger 'Dijkzigt Hospital' in 1961. The national government decided in 1965 that a medical faculty was needed and it should be located at the Erasmus University, which until then had rested only on economics and law schools. The university opened in 1973 and originally comprised a medical faculty and a school for economics. The Academic Hospital Rotterdam was opened in 1967; the Sophia Paediatric Hospital has served as the university paediatric department since 1971.

Jan Willem Ter Braak (1903-1971) obtained the physician's license in Amsterdam and specialised in neurology under Brouwer. He completed his training as a neuropsychiatrist under Carp in Leiden, but favoured the field of neurology. He became assistant to Rademaker in Leiden and practiced in The Hague. After World War II, he moved to Rotterdam and became extraordinary professor of neurology at the University of Leiden (1961) with an inaugural address on "The object of the neurologist." The chair was established in particular for the Foundation of Clinical Higher Education in Rotterdam. Ter Braak was asked to become full professor of neurology when the medical faculty was founded, but he did not accept the offer until 1967. Unfortunately, he suffered a serious heart attack in 1968 and had to resign in 1970. *Arthur Staal* became the first ordinary professor of neurology in 1970 and was succeeded by *Van der Meché* in 1991.

Table VIII. Professors of Neurology in Rotterdam.

Professor	Chair	Period
J.W.G. ter Braak (associate)	Neurology	1957-1970
H. van Crevel (interim)	Neurology	1968-1970
A. Staal	Neurology	1970-1991
F.G.A. van der Meché	Neurology	1991-2001

Maastricht

The University of Maastricht was founded in 1976 and is known in the Netherlands for its special didactic approach (also referred to as problem-orientated teaching), using teacher defined 'problems' as a starting point, rather than textbooks. The medical faculty was the first to be developed according to this principle and gradually other medical curricula in the Netherlands are being modelled after the Maastricht method. With respect to research in neurology and psychiatry, there is an emphasis on aging, in particular its effects on cognition.

Paul van der Lugt (1936-1990) received his neurology training from ter Braak in Rotterdam, where he held a position as staff member. In 1979, he became head of the newly founded neurology department in Maastricht. *Jaap Troost* succeeded him in 1992 (until 2001).

Table IX. Professors of Neurology in Maastricht.

Professor	Chair	Period
P. van der Lugt	Neurology	1979–1990
J. Troost	Neurology	1992–2001

Epilogue

What kind of picture arises from all these names and dates, representing the development of neurology at the Dutch universities? Winkler was important as he promoted psychiatry and neurology as academic subjects in the Netherlands. Partly due to his orientation on German neuropsychiatry, he was in favour of teaching psychiatry and neurology as one discipline. In 1923, the first separation of a chair of neurology and psychiatry occurred in Amsterdam. Winkler's pupil Brouwer, who took the new chair of neurology, became the second man in Dutch neurology. He introduced the American style of neurosurgery to the Netherlands. Winkler and Brouwer determined the direction of neurology, both as a clinical and as a scientific discipline. Also in the sense that they taught a large number of students who later dispersed and got important positions. The first half of the 20^{th} century was characterised by the complicated debate on the relationship between psychiatry and neurology. Leading neuropsychiatrists pleaded for a combination, the kind of neuropsychiatry that found its origin in Germany. Consequently, it was a long time before independent neurological departments and clinics had been created at the universities. Another consequence was that the opportunities to set up basic and good clinical research programmes were limited. Research flourished more outside the academic centres.

Future research on the history of academic neurological centres could focus on numbers of members of staff and trainees, numbers of beds, outpatients and clinical patients, facilities such as CSF laboratories, and development of specialised units (e.g., neuropediatrics, neuropathology). This would complete the picture of the development of neurology in the academic centres.

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The Extra-Academic Centres 3

P.J. Koehler

Along with what happened in academic neurological centres, an important evolution took place at extra-academic centres. These include two categorical neurological hospitals (Alexander van der Leeuw Clinic, Amsterdam, and Ursula Clinic, Wassenaar), three epilepsy centres (Hans Berger Clinic in Breda, Kempenhaeghe in Heeze, and Meer en Bosch in Heemstede), five neurological training departments (Amsterdam, The Hague, Heerlen, Nijmegen, Tilburg) and finally the Netherlands Institute for Brain Research (Amsterdam). Clearly, neurology was also practised at other hospitals, but I have chosen the five departments where a full training in neurology is provided, as these probably had more influence on Dutch neurology than the others. The history of these centres will be described up to the 1970s, when the present generation of neurologists gradually deployed their professional activities. As the history of some of the centres described below is older than others, the sections on the various centres differ with respect to length and contents.

Most of the physicians, who will be mentioned in this chapter, worked in the joint field of neurology and psychiatry. I have chosen to use the English term neuropsychiatrist for this chapter as they were called 'zenuwarts' (nerve-physician) in Dutch. However, the term should not be confused with the present term.

1 Alexander van der Leeuw Clinic

Figure 1. Louis Jacob Joseph Muskens (1872-1937).

The Dutch 'Society against Falling Sickness' was founded in The Hague in 1902. In contrast to the 'Christian Society for the Care of Sufferers of Falling Sickness', founded in 1882 (see *Meer en Bosch*), the main object of the new society was not the *care*, but the *treatment* of epileptic patients, whenever possible in the initial stage of the disease (Huddleston Slater 1932, p. 187-191). The goal was to be reached by establishing one hospice and several outpatient clinics disseminated over the country. A specialised hospital was founded at the Overtoom in Amsterdam in 1903: the 'Amsterdamsche Gasthuis tegen vallende ziekte' (i.e., hospice for epilepsy). The number of beds increased from six (1903) to twenty in 1916. Louis Jacob Joseph Muskens (1872-1937, figure 1) became the first medical superintendent. He had written his thesis in 1896 under Theodor Engelmann (1843-1909), the son-in-law and successor to the chair of physiology of Franciscus Cornelis Donders (1818-1889) in Utrecht: *On the reflexes of the cardiac ventricle on the heart of Rana*. Muskens received a scholarship of the Donders Foundation, which enabled him to go to the United States, where he worked under Charles Loomis Dana (1852-1935), who was professor of diseases of the nervous system at Cornell University Medical College in New York. He also worked in London with William Richard Gowers (1845-1915) and Victor Horsley (1857-1916). He became private teacher of diseases of the nervous system in Amsterdam in 1906. Three years later, he founded the International League against Epilepsy in cooperation with the Hungarian Donath. Muskens was secretary-general of that organisation from 1909 until 1937. He published numerous papers in German and Dutch journals (a few in American journals as well) on various neurological subjects, including the supra-vestibular system, and a book on epilepsy: *Epilepsie: vergelijkende pathogenese, verschijnselen, behandeling* [Epilepsy: comparative pathogenesis, phenomena, treatment] in 1924. A German translation appeared two years later in the series *Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie*. It includes the results of experimental (1899-1916) as well as clinical studies (1900-1923) on epilepsy. Muskens was an advocate of separate epilepsy clinics, similar to the London National Hospital for the Paralysed and Epileptic and Craig Colony in New York State (Eling 2000).

Following a donation by the Maecenas, Alexander van der Leeuw, and an important contribution from the government, a new clinic with 42 beds, which was named after its sponsor, was opened in 1922. In the meantime, several epilepsy outpatient clinics had been established in Amsterdam (1903), Arnhem, Rotterdam, Utrecht, Zwolle and Leeuwarden (1915).

Jacobus Josef Hubertus Maria Klessens (1888-1972), who had trained under Cornelis Winkler (1855-1941) and Johannes Karel August Wertheim Salomonson (1864-1922), succeeded Muskens in 1918. Klessens had written his thesis in 1913, following a two-year period at the physiological laboratory of Gerard Abraham van Rijnberk (1875-1953): *The representation fields of the spinal nerves in the skin of the cat, as determined by the strychnin-isolation method*, applying Dusser de Barenne's method. Klessens remained superintendent until 1953.

Following World War II, some of the epilepsy outpatient clinics were exploited in co-operation with the Christian Society for the Care of Sufferers of Falling Sickness. A few outpatient clinics became independent.

Albert Marie Lorentz de Haas (see below) succeeded Klessens as medical superintendent in 1953, however, he left two years later to become medical director of *Meer en Bosch* epilepsy institute. Willem Anton den Hartog Jager (1914-1993) succeeded him in 1955. He was interested in the cerebro-vascular genesis of diseases that resembled epilepsy and he started admitting patients suffering from cerebro-vascular accidents. Arie Biemond (see chapter 17) was scientific supervisor during the 1960s and the Van der Leeuw Clinic became associated with the neurological department of the Wilhelmina Gasthuis. In cooperation with Biemond, Erik Joseph Everard Frohn (1925-1970), who succeeded Den Hartog Jager as director in 1961, started admitting patients suffering from cerebral tumours, often a cause of epilepsy. In this way, the

Alexander van der Leeuw Clinic gradually lost its categorical character. It started as a hospice for epileptics and gradually other patient categories were admitted, including multiple sclerosis (added in the 1970s), cerebrovascular diseases and cerebral tumours. Leo W. Zoeter succeeded Frohn following his untimely death in 1970. Norbert F.J. Hanke was the last superintendent until the clinic was shut in 1987 and merged with the Amsterdam St. Lucas hospital (Hanke 1977).

2 Ursula Clinic

Figure 2. J.M.J. Tans (1911-1990).

One of the main reasons for starting the original St. Jacobus Stichting (foundation) in 1923 was the fact that there were no Roman Catholic psychiatric clinics in the city of The Hague. Protestants had founded 'Bloemendaal' in 1892 and the mental hospital "Oud-Roozenburg" did not have a confessional bond. Psychiatric patients could not be admitted to the 'H. Johannes de Deo' Hospital, although a neuropsychiatrist was practising there. An estate for the new clinic was purchased in Wassenaar, a town to the north of The Hague. Eduardus Quirinus Hoelen (1896-1962), trained by Leendert Bouman (1869-1936) in Amsterdam, became its first director.

In the early 1930s, plans were made to expand the clinic, in particular with the aim to establish separate neurological and neurosurgical wards. It took until 1936 to have the plans realised. On 6 June 1936, the new building complex, the St. Ursula Clinic, was opened, enabling neurological patients to be submitted to a neurological ward instead of psychiatric wards. Arnold C. de Vet (1904-2001) performed the first neurosurgical procedure in the same year. Ignaz Oljenick (1888-1981), the first Dutch neurosurgeon (trained by Harvey Cushing [1869-1939]), had trained him at the Wilhelmina Gasthuis in Amsterdam. De Vet was assisted by J.M.J. Tans (1911-1990, figure 2), neuropsychiatrist, who succeeded Hoelen as director of the clinic in 1961. Later, a second neurosurgeon P.R.M.J. Hanraets (1904-1995) was appointed. In this way, the Ursula Clinic became the fourth Dutch neurosurgical clinic in the Netherlands, the other three being university departments (Amsterdam, Utrecht and Groningen). De Vet introduced cerebral angiography in the Netherlands (1936), following its discovery by Antonio Caetano de Egas Moniz (1874-1955) in 1927.

Otto Magnus, who trained in London (William Grey Walter [1910-1977]) and Montreal (Herbert Henri Jasper [1906-1999] and Wilder Penfield [1891-1976]), became the first clinical neurophysiologist at the Ursula Clinic in 1949 after the clinic's first EEG machine had been purchased. One-channel EEGs had been performed by the assistant psychiatrist L.J. Franke since 1935, who wrote a thesis on EEG in 1942.

Between 1946 and 1961, several prefrontal leucotomies were performed at the Ursula Clinic. The number of neurosurgical procedures increased to over 1000 per year and the Ursula Clinic became well known internationally. It also became the teaching hospital for many neurologists, neurosurgeons and psychiatrists.

In 1950 a clinic for paediatric neurology and neurosurgery was added. In March 1979, the neurological and neurosurgical departments moved to the new Westeinde Hospital in The Hague, while the psychiatric departments remained. The training of neurologists continued at that new hospital (Hoelen-v.d. Pol 1980).

3 Extraneous neurological departments

AMSTERDAM

St. Lucas Hospital opened in 1966 and started with two departments, one for internal medicine and the other for neurology. B.J.J. Ansink and Mrs. C.J. Snijders were the first neurologists. Training permission was obtained in 1968 (B) and 1972 (A). G.P.M. Horsten performed the first EEGs. A. Kropveld was appointed clinical neurophysiologist in 1967. The department of clinical neurophysiology obtained permission for training in 1980 (A. Zonneveldt). In 1976 a specialised aphasia centre was opened as a part of the rehabilitation department. Neurosurgery started in 1973 when H.A.M. van Alphen joined the staff at St. Lucas Hospital. He became professor of neurosurgery at the Vrije Universiteit in 1978. A second neurosurgeon joined in 1975 (R.E.H. van Acker).

THE HAGUE

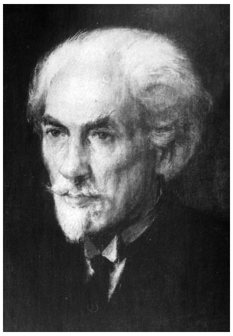

Figure 3. Gerard Christiaan Bolten (1872-1941).

The first neurologist at the Municipal Hospital of The Hague 'Zuidwal',), Gerard Christiaan Bolten (1872-1941, figure 3) was appointed on February 1, 1910. Bolten had studied medicine in Utrecht, where Winkler was professor of psychiatry and neurology (until 1896), and became medical director of the newly built psychiatric asylum 'Oud-Roozenburg' in The Hague in 1900. He resigned in 1904, starting a private practice of neurology. Meanwhile he offered voluntary neurological consultations to the Municipal Hospital. He was appointed neuropsychiatrist in 1910, but devoted most of his time to neurological patients. It is obvious from his bibliography that his scientific interest was mainly in the field of neurology. He published on various subjects including two patients suffering from Landry's paralysis (Bolten 1910). He did not find inflammatory cells in the cerebrospinal fluid and described yellow protein-rich fluid, six years before Guillain and Barré described the *dissociation albumino-cytologique*. In cooperation with the surgeon C. Schoemaker, he published on neurosurgical procedures. A number of papers dealt with epilepsy. In 1934 he published a psychiatric report on Marinus van der Lubbe, who set the *Reichstag* in Berlin on fire. The German police wanted to arrest Bolten in 1941, but he died a few months earlier in November 1940, after he had retired from the Zuidwal Hospital in 1939 (Endtz et al. 1984).

Jan Willem Gijsbertus ter Braak (1903-1971), Wim to his friends, was appointed neuropsychiatrist in November 1938. He had been trained for neurology by Bernardus Brouwer (1881-1949; see chapter 19) in Amsterdam and wrote a thesis on *Clinical-anatomical investigation on neurological respiratory abnormalities*. Between 1934 and 1939 he performed experimental neurophysiological work at Rademaker's laboratory in Leiden. Ter Braak noted that the psychiatric work in the Zuidwal Hospital consisted mainly of consultations to assess whether a patient could stay in the hospital or had to be transferred to a psychiatric asylum. A large neurological ward was opened in 1941 and as from 1950, the psychiatric consultations were carried out by a psychiatrist. Ter Braak presented a pragmatic approach to the relationship between neurology and psychiatry: "A grocer, who next to his merchandise sells a book once or twice, remains a grocer, but as soon as the books in stock will attract spoiled bibliophiles, I call him bookseller, even if at times he would sell a pound of sugar..."

Like many people in those days, Ter Braak suffered under the German occupation. His brother, the well-known writer Menno, committed suicide because of it in 1940, and in 1942, Wim was arrested for refusing to cooperate with the transport of Jews from the hospital. He was imprisoned in Vught for a period of six months. In the post-war period, Ter Braak started the study of eye movements that so intrigued him. In 1954, he left for Rotterdam, where, after the opening of a medical faculty in 1965, he became professor of neurology in 1967. Following his retirement in 1970, he passed away in 1971, behind his desk at the physiological laboratory, still doing scientific work (Endtz et al. 1984).

Antonie Verjaal (1910-1973) succeeded Ter Braak at the 'Zuidwal' in 1954. He had studied medicine in Utrecht and Groningen, and trained for neurology and psychiatry in Utrecht under Leendert Bouman. He wrote a thesis on amnesia following head trauma and worked at the epilepsy institute 'Meer en Bosch' until he was appointed at the Zuidwal Hospital, where he worked until he was called to take the chair of neurology at the University of Leiden in 1970. He published on epilepsy, aphasia and cerebrospinal fluid pressure (Lindeboom 1984). Although training neurological residents at a peripheral hospital, he demanded scientific research and if possible publications. He had an extensive knowledge of the neurological literature, which he summarised on cards that he arranged systematically. As a teacher he was demanding, he liked simplicity and clarity (Endtz 1984).

Lambertus Jacobus Endtz (1926-1989) studied medicine in Leiden, where he also trained in neurology under Gijsbertus G. J. Rademaker (1887-1957). In 1959-1960 he worked as a 'médecin résidant étranger' at the Salpêtrière in Paris. He wrote his thesis on blood pyruvate in neurological afflictions (1963). Starting in 1961 he worked at several hospitals in The Hague until he succeeded Verjaal at the Zuidwal Hospital in 1970. In 1972, the neurological department moved to the new building, the Leyenburg Hospital, where he remained until his untimely death in 1989. Endtz practised neurology in the classical way. Taking the history and examining the patient in the way he had learned at the Salpêtrière, were his most important instruments. He stimulated his residents to perform scientific work, which he considered of great importance, even in a peripheral hospital. Next to his neurological publications, he was interested in the history of medicine, which resulted in various papers and books (Schulte 1991).

Starting in 1939, a continuous stream of neurologists (-psychiatrists) was trained by Ter Braak, Verjaal and Endtz. The scientific production of the department throughout the 20th century was considerable.

HEERLEN

Brother Aloysius of the congregation of St. Joseph in Heerlen was sent to Wörishofen in Bavaria in 1891 to learn about the water cures of Sebastian Anton Kneipp (1821-1897), developed in particular for patients with a weak nervous system. The main reason for his mission was to help the numerous epileptic patients at the confessional hospices in Heerlen. Upon his return to Heerlen, he started a sanatorium in 1892. As the cure appeared to have disadvantages as well, F.B.M.B. Schiphorst, the first neuropsychiatrist in the region, was invited to examine the patients in the sanatorium prior to the cure. He was appointed in 1917 and dealt mainly with neurotic patients. He wrote his thesis *On the aetiology and symptomatology of tabes* in 1920 and in 1925 he started consultations at the St. Joseph Hospital. The hospital was built in 1904 and neurological as well as psychotic patients were admitted. Meanwhile, he continued to treat neurotic patients at the sanatorium. T. Kuiper, who wrote his thesis *Die funktionellen und hirnanatomischen Befunden bei den japanischen Tanzmaüse* (approx. 1912) under Cornelis Winkler, had been neuropsychiatrist in Heerlen for a short time before Schiphorst was appointed at the hospital. Schiphorst's main field of interest was psychiatry. Suffering from diabetes mellitus he developed cognitive deficits, a reason why De Jong was invited to come to Heerlen.

Johannes Gerardus Ype de Jong (1909-1998, figure 4), son of an engine driver for the Dutch Railway, came to Heerlen in February 1941. He studied medicine (on a so-called colonial contract) in Utrecht, obtaining his MD in 1933, but was never sent to the East Indies. He subsequently trained to become a neuropsychiatrist (1933-1936) under L. Bouman. He started a practice at the Calvarienberg Asylum in Maastricht in 1936, appointed by the City Council. He moved to Heerlen in 1941, hoping to have his own neurological-psychiatric department. Upon his arrival, he found a declining department, as Schiphorst had been ill for some time. However, psychiatric and neurological nursing was still well organised. During World War II, De Jong was the hospital's contact person for the physician's resistance and he hid Jews during the War. He went into hi-

Figure 4. J.G.Y. de Jong (1909-1998).

ding in 1943, reading Bumke and Foerster's 17-volume *Handbuch* from beginning to end.

Following the war, De Jong established a flourishing psychiatric and neurological department and published several important papers, among which "On families with hereditary disposition to the occurrence of neuritis, correlated to migraine" (De Jong 1947, originally in Dutch), the first description of hereditary liability to pressure palsy, the genetic origin of which has been identified on chromosome 17. He also described Myotonia Levior, demonstrating the patients to P.E. Becker. In 1949, he made a three-month study tour to the United States, visiting Boston, New Haven, Baltimore, New York and Washington. He wrote his thesis *Dystrophia myotonica, Paramyotonia and Myotonia Congenita* (1955) guided by W.G. Sillevis Smitt.

De Jong started training residents in the 1940s and was instrumental in establishing a neurosurgical department at the St. Joseph Hospital in 1956, when Louis Coene, the first neurosurgeon, was appointed. In the following year, Jan Mol started a neurophysiological department, at first using a primitive EEG apparatus in a house near the hospital. Following the expansion of the hospital he moved into the new buildings. H.J. Kreutzkamp became resident in 1954 and was appointed as neuropsychiatrist in 1960. F.H.M. van der Maessen de Sombreff came a few years later. Cor C. Hagen was appointed in 1968 and Jan Frans Mirandolle in 1970. In 1974, the very year that the Netherlands Society of Psychiatry and Neurology dissolved into two separate societies, neurology and psychiatry at the Heerlen hospital were separated following the opening of the nearby psychiatric asylum, 'Welterhof'. Kreutzkamp and Van der Maessen de Sombreff moved to the asylum, whereas Hagen and Mirandolle stayed in the hospital. De Jong retired in 1975. (De Jong 1954, pp. 143-6; Hendriks & Brun 1979, pp. 54-7 and 76-8; J.M. de Jong, personal communication, 15 Sept. 2000.)

NIJMEGEN

When Dr. J.J.G. Prick (1909-1978) came to Nijmegen in 1940, two neuropsychiatrists were already employed at the St. Canisius Hospital, which opened in 1926: J. Wiardi-Beckman (employed from 1926 until 1938) and J. Hardon (from 1938 until 1940). Prick was working at the Municipal University Hospital of Amsterdam when he was invited to come to Nijmegen, and he was promised that he would soon have a neurological and psychiatric department at his disposal. The new clinic was to become the first institute of the medical faculty. However, the war would result in a delay of these plans and he only had a small 'nerve-pavilion' at his disposal. Nevertheless, he was asked to read forensic neuropsychiatry at the faculty of law in 1941. Still during the war period, a more spacious clinic became available at the Brakkestein villa.

Initially, Verbeek, neurosurgeon in Groningen, came to Nijmegen for neurosurgical procedures once a month. In 1942 a full position for a neurosurgeon became available for P.M.J.J.P. Hoebrechts (employed from 1942 until 1951). J.J. Prick was invited by his cousin J.J.G. Prick to come to Nijmegen in 1947. The psychiatric and neurological clinic already had training facilities when he arrived, and he was the only resident when he arrived. He became responsible for patient care at the neurology, neurosurgery and psychiatry departments, as his cousin was fully occupied with educational and organisational work, i.e., the preparation for an academic hospital at the medical faculty, which was started from and in association with the St. Canisius Hospital (Prick 1994). St. Canisius Hospital therefore had several academic functions at first. The lecture room was built there and paid for by the university. For EEGs, patients had to be transported to Arnhem (Dr. A.P. Heystee), until Pieter Bernsen, who became a resident in 1951, started electrophysiology in a small room underneath the lecture room. When academic neurology and J.J.G. Prick moved to the new buildings of the St. Radboud Academic Hospital in 1956, J.J. Prick became superintendent of the department of psychiatry and neurology. He also became acting chief of psychiatry and neurology at the Academic Hospital. The neurological departments of the St. Canisius Hospital and the St. Radboud University Hospital became one functional unit in particular with respect to the training facilities for residents, with J.J.G. Prick as instructor, which was approved by the Specialist Registration Committee. (Prick 1975) E.F.J. Poels joined the staff in 1976 and M.J.J. Prick in 1981. In 1983, when C.W.G.M. Frenken succeeded J.J. Prick, two independent neurological departments were established with two training recognitions.

TILBURG

Figure 5. J.L.M. Sinnige (1906-1972).

Following the opening in 1929, A. de Ruyter, neuropsychiatrist from Breda, started consultations at the new St. Elisabeth Hospital in Tilburg. Neurological patients were still admitted to the internal ward until 1941. J.L.M. Sinnige (1906-1972; figure 5) settled in Tilburg in 1940 and brought into effect the first neurological-psychiatric department. Sinnige trained in Amsterdam with Bernard Brouwer and Klaas Herman Bouman (1874-1947) and wrote his thesis on *Anatomical investigation on the connections of the cerebellum of the dog* (1938). He remained in contact with Brouwer's successor Arie Biemond, with whom he published several papers and who sometimes came to Tilburg to examine difficult patients. When De Ruyter retired in 1946, the first resident, J. Taverne, was appointed at the neurological-psychiatric department. This event marks the start of neurological training in Tilburg. Taverne became neuropsychiatrist at the second neurological-psychiatric department of the hospital in 1951, the year in which the neurosurgical department was opened. M.P.A.M. de Grood, who trained with C.H. Lenshoek and W. Noordenbos in Amsterdam, was the first neurosurgeon. Sinnige and De Grood are considered the founders of the neurological and neurosurgical departments of the St. Elisabeth Hospital. In the same year, the first EEG apparatus was introduced. J.H.van Luijk was appointed neuropsychiatrist, in particular for electro-encephalography and neuroradiology (1954). He had trained with Otto Magnus and may be considered the pioneer of EEG in the southern Netherlands, as he taught the principles of EEG to colleagues in the region. Following the retirement of Sinnige in 1958, Van Luijk took over his neurological practice. Nevertheless, Sinnige remained supervisor of the neurological-psychiatric training until 1965, by which time he had trained 25 neuropsychiatrists.

Bento P.M. Schulte, who had trained at the Ursula Clinic, succeeded Taverne in 1960. Meanwhile, Van Luijk had received EEG teaching qualification in 1959 and neurological residents could now do their EEG-qualification in Tilburg. After the first and second neurological-psychiatric departments merged in 1967, Schulte became instructor in 1969, by which time the department had been without teaching qualification for four years. The staff increased to four in 1976. Schulte and Leyten conducted an extensive epidemiological investigation on stroke in Tilburg (TESS) between 1978 and 1981. Meanwhile, Schulte was called for the chair of neurology at the Catholic University of Nijmegen in 1979, and was succeeded by Dolf op de Coul (1932-2000) in 1980 (Op de Coul 1991).

4 Epilepsy clinics

DR. HANS BERGER CLINIC

'De Klokkenberg', near the city of Breda, was originally a sanatorium for tuberculosis patients. When the number of patients decreased at the end of the 1950s, the administration looked for new opportunities and met J.H. Bruens, neuropsychiatrist at the Laurentius Hospital in Breda, who had plans to start a clinic for patients suffering from epilepsy. The Inspector of Mental Healthcare gave the go-ahead under the condition that they would cooperate with the Providentia Institute in Sterksel (see below). The 'Brothers of the Holy Joseph' had founded this institute in 1920 (see section on Kempenhaeghe).

At the Klokkenberg, measures were taken for the particular care of epilepsy patients. Facilities for examination, treatment, labour, education, sport and games were set up. An EEG department was started and the number of patients gradually increased to 110, sixty of whom were children. A special ward for thirty adolescents was added. In 1965, the new epilepsy clinic was named after Hans Berger (1873-1941), the discoverer of the human EEG (1929). Stereotactic operations were carried out at the Klokkenberg, where in the meantime a centre for thoracic surgery had been founded. Three epilepsy outpatient-clinics were started in Rotterdam, Goes and Terneuzen (P. Voskuil, written communication, August 2000). The following neuropsychiatrists worked at the Klokkenberg: J.H. Bruens (born in 1923), J.W.M. Jongmans, prof. C.H.M. Brunia (born in 1932) and A.E.H. Sonnen (1931-2000).

KEMPENHAEGHE

In 1919, the Brothers of the Holy Joseph in Heerlen decided to start a new foundation in Heeze in the northern part of the province of Limburg. Brother Aloysius, superior of the congregation, who was caring for epileptic patients in the Sanatorium in Heerlen (see section on Heerlen), was one of the clerics who visited Sterksel, after which the council decided to buy an estate and build a new home for the care of epileptics. The first simple convent was opened in 1920 and seven years later a larger building was opened: Huize Providentia. Fifty patients and thirteen male nurses moved into the new building. Kwishout, the local physician, provided medical care. A paediatric department was added in 1936. Meanwhile, the first laymen nurses were employed in 1932. During the war in 1942, the Germans ordered the institute to be cleared. Following the liberation in September 1944, the English used the buildings as a hospital and the institute came into function again in 1946. Kwishout's successor J.E.H. Rutten, who had become medical director in 1942, was instrumental in reorganising the institute after 1946. In 1953 plans were made to start the first Roman Catholic institute for female epilepsy patients in the Netherlands. The Franciscan congregation was prepared to care for the patients and in 1958 a new foundation was established, 'Catholic Foundation for Epileptics in the Netherlands'. Lorentz de Haas from Meer en Bosch and De Vet from the Ursula Clinic were members of the medical advice committee. The new institute, Kempenhaeghe was built in 1962 and would cooperate with the Klokkenberg institute of Breda. Providentia and Kempenhaeghe merged into one foundation in 1964, the year in which Kempenhaeghe was officially opened. The number of patients increased and in 1966 Providentia had 282 patients and Kempenhaeghe 137 patients. Starting in 1970 both institutes became organised in one foundation and the integration started. Finally, Providentia would become the residence for chronic patients.

The neurologist R.J.E.A. Höppener succeeded P.F.M. Houben, neuropsychiatrist, who had worked at the institute for ten years. In 1975 J.H. Bruens, clinical neurophysiologist, was succeeded by A.C. Declerck. Moreover a new neurologist (R.T.M. Starrenburg) was appointed in that year. After serving for 27 years, Rutten retired in 1978. L.F.B. Schooleman succeeded him as medical director. Outpatient-clinics for epilepsy were started in Enschede and Sittard (Frissen 1983).

MEER EN BOSCH

Following the example of the Bodelschwinger Anstalten in the German town of Bielefeld, the Christian Society for the Care of Sufferers from Falling Sickness was founded in 1882 on the initiative of the noble lady A.J.M. Teding van Berkhout (1883-1909) and in the same year a small home for a few women suffering from epilepsy was opened near the town of Haarlem: Zoar, after the biblical place of refuge for Lot. Two years later a larger building, Bethesda, was opened, and in 1885 Meer en Bosch, near Heemstede, was bought and furnished for the care of epileptic men. Throughout the following years, new buildings were built on both properties. The local general physician was responsible for the medical care at the institutions. He provided service on a voluntarily basis. In 1897 a neuropsychiatrist was found: J. Timmer, former physician in the Psychiatric Asylum of Utrecht. M. Colenbrander, general physician in Heemstede succeeded him at Meer en Bosch in 1901. He made a study tour in Germany (1903) and experienced that their care for epileptics at Meer en Bosch was not lagging behind that of the foreign institutes, except for the use of baths and handicrafts.

In 1890, the number of patients at Meer en Bosch was 57, cared for by 20 male nurses, and in 1912 these numbers had increased to 212 and 90 male nurses. In Bethesda Sarepta, 54 nurses cared for 196 patients. The nurses were trained at the institution, although some were sent to Bielefeld during the first years. A few went to Amsterdam (Wilhelmina-Gasthuis) for training in general nursing and some to Santpoort for psychiatric nursing. Gradually, the need of a private physician was felt and in 1906, C.J.C. Burkens took up residence in the new physician's house, but later he moved to Haarlem, from where he served both institutions (Meer en Bosch and Bethesda Sarepta). He remained physician of the institutes for 22 years. During a period of illness, Gerard Christiaan van Walsem (1863-1935), who had been professor of medicine in Leiden (1901-1904) and medical superintendent at the Meerenberg psychiatric asylum replaced him. Johan van der Spek succeeded Burkens in 1927. Next to the care of the patients, the physicians assignment was also the teaching of the nurses.

At the celebration of the 50th anniversary in 1932, the number of epileptics in the Netherlands was estimated at 14.000, half of whom needed care. Four hundred were being cared for in the buildings in Haarlem and Heemstede. It was recalled that over the years, the number of seizures and the mortality due to status epilepticus had decreased considerably, due to medical treatment. Whereas status epilepticus had had a mortality of over 50 per cent, the figure had diminished to zero in 1927, as Van der Spek wrote in the records of that year. Van Walsem compared the number of seizures in 1922 (12.703 in 220 patients) to 1926 (3.684 in 240 patients), i.e., a decrease from 58 to 15 per patient per year (Gedenkboek 1932, p. 83). Next to medical treatment the patients were treated by labour therapy. Ledeboer recalled that only bromide remained an important medication throughout the years, although the risks of bromism were realised (Ledeboer 1932, p. 154). Opium (sometimes in combination with bromide), atropine and chloralhydrate were also used at the time, though the most important drug in 1932 was luminal (introduced in 1912). Leendert Bouman mentioned surgical therapy for some patients suffering from Jacksonian epilepsy (Bouman 1932, p. 173). Winkler in Utrecht, in cooperation with the surgeon Guldenarm, had already treated patients by surgery for epilepsy around 1890. Although the institution was often a temporary home for epileptics without mental disturbances, those who were mentally deranged stayed for the rest of their lives.

When Van der Spek left and became director of the Maasoord psychiatric asylum in Poortugaal (near Rotterdam) in 1930, he was succeeded by B.Ch. Ledeboer, who was appointed directing-physician of both institutions, and by R. Burdet who became physician in Bethesda Sarepta. Ledeboer was the first physician to become director, as clergymen had been in charge until then. In May 1934, the Queen Emma Clinic was opened and two years later, a second physician was added to the staff (Antonie Verjaal, see also section on The Hague). Paediatric epilepsy was among

Ledeboer's most important fields of scientific interest. He finished his thesis on the subject under Rümke (Utrecht, 1941). During the war, in 1942, the institutes, Bethesda Sarepta and Meer en Bosch, came under NSB (National Socialist Union, an organisation collaborating with the Germans) administration. However, their families took the patients home and the staff refused to stay (Oostenrijk 1970, p. 90). Meanwhile, travelling male nurses took care of the patients while they were staying with their families. Some of these nurses were already active before the war and they had organised the epilepsy outpatient clinics (the first in Apeldoorn, 1924), The original administration, the direction and the personnel remained organised to this purpose between 1942 and 1945. Following the liberation, 500 wounded German soldiers had to be transported from Meer en Bosch before it was taken over again by the epilepsy institute in June 1945.

Meanwhile, Otto Magnus, who also worked at the Ursula Clinic, introduced the first EEG apparatus at Meer en Bosch in 1948. He had a part-time appointment from 1950 until 1968. In cooperation with De Vet, neurosurgeon, epilepsy surgery was performed (1950-1960), at first at Meer en Bosch, later at the Ursula Clinic.

Albert Marie Lorentz de Haas (1911-1967; figure 6) became medical director in 1955. He was the grandson of physicist and Nobel prize winner Hendrik Antoon Lorentz (1853-1928). He trained under psychiatrist Hendrik Cornelis Rümke (1893-1967) and Brouwer in Amsterdam, and had been medical director of the Alexander van der Leeuw Clinic in Amsterdam for some years. Under his direction, the number of scientific papers grew considerably and Meer en Bosch became one of the leading epilepsy clinics of the world. In 1966, the Cruquiushoeve, a commune for chronic epilepsy patients, who had an additional physical or mental handicap, was opened (Lorentz de Haas 1967).

Figure 6. Albert Marie Lorentz de Haas (1911-1967).

A triumvirate of directors succeeded Lorentz De Haas in 1968: Lambertus Stoel, clinical director, Harry Meinardi (1932-), scientific director, and Hen Wefers-Bettink, personnel director.

5 Brain Institute

The International Academic Committee for Brain Research was founded in 1904, following a proposal by Wilhelm His (1831-1904) during the meeting of the International Association of Academics in Paris (1901). The aim of the new organisation was to organise "a network of institutions throughout the civilised world, dedicated to the study of the structure and functions of the central organ…" One of the advices of the Committee was to found Institutes for Brain Research and to unite existing institutes. Cornelis Winkler and Louis Bolk (see chapter 18) drew up a report on the basis of which permission was obtained to found the Central Institute for Brain Research in Amsterdam, in a wing of the Department of Anatomy and Embryology of the University of Amsterdam. It was opened on June 8, 1909, and C.U. Ariëns Kappers, well known for his work in the field of comparative neuroanatomy, became the first director (see chapter 16). A number of human and animal brains, 'the Ariëns Kappers Collection', have been preserved at the institute. The collection includes 500 specimens of formalin-fixed whole brains and approximately 30,000 sections of brains of over 300 species of vertebrates. Bernard Brouwer succeeded him in 1946. One of his collaborators, J. Droogleever-Fortuyn, introduced electrophysiology into the research programme. The institute was reorganised following Brouwer's death in 1949. A multi-disciplinary approach to brain research was now applied. Siegfried Thomas Bok (1892-1964) was appointed director in 1952. He had studied medicine in Amsterdam, during which period he had already worked at the Brain Institute. He had qualified in 1916 and, following the end of the mobilisation period in 1918, had been appointed assistant-neuropathologist at Leendert Bouman's laboratory of the Valerius Clinic. Bok wrote his thesis *On the ontogenesis of the spinal cord reflex apparatus with the central relations of the sympathetic nerve* (1922) under Cornelis Winkler. He was appointed professor of medicine at Leiden University in 1929, assigned to teach histology and microscopical anatomy. In 1951 he became Rector of the University and the following year he was appointed director of the Brain Institute in Amsterdam. Bok published several books, including *Die Histopathologie des Zentralen Nervensystems* (1931; in cooperation with L. Bouman), and *A quantitative analysis of the structure of the cerebral cortex* (1936). He is considered to belong to the pioneers of the quantitative morphological analysis of the brain, in particular the cortex. He retired in 1962 and was succeeded by J. Ariëns Kappers (nephew of C.U. Ariëns Kappers), who studied, in particular, the circumventricular organs, and with his collaborators, the pineal gland. The name of the institute was changed to the Netherlands Institute for Brain Research in 1976 and D.F. Swaab, though acting director since 1975, was appointed director two years later. He became extraordinary professor of neurobiology in 1979. The institute moved to the Academic Medical Centre of the University of Amsterdam in 1984 (Van Pelt et al. 1998).

Conclusion

Reviewing the institutes that have been discussed in this chapter one may conclude that the care for epileptics played an important role in motivating the foundation of extra-academic institutes. In some cases, religious motives led to the establishment of additional centres. Whereas care was the principle aim of the epilepsy institutes at the start, the emphasis gradually changed to cure and physicians were appointed as superintendents.

The importance of extra-academic centres for the training of neuropsychiatrists can be demonstrated by the history of the Ursula Clinic and the Municipal Hospital in The Hague. These were the first to start peripheral training facilities for neuropsychiatrists in the 1930s. Throughout the years a considerable number of neuropsychiatrists were trained here and their scientific production cannot be neglected. Some of the neuropsychiatrists trained there became professors at academic hospitals. These neuropsychiatrists put an important stamp on Dutch neurology.

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The Netherlands Society of Neurology

4

D. van der Most van Spijk

The following review of a number of historical developments that preceded the birth of the Netherlands Society of Neurology on 1 January 1974 will be helpful in gaining a clear understanding of the current organisation of the specialism of neurology. Its predecessor was the Netherlands Society of Psychiatry and Neurology, and in particular the Chamber of Neurology, which, together with the Chamber of Psychiatry, constituted the aforementioned Netherlands Society. Following the division (in 1962) into chambers, the board of the overall society was referred to as 'the Main Board'. For some time, the undersigned had a seat on the Main Board as representative of the Chamber of Neurology, and was chairman of the new Netherlands Society of Neurology from 1 January 1974 for a period of four years. He was in a position to participate in the discussions that culminated in the current organisation, and subsequently to be the first to put it to the test in practice.

It is interesting to identify the role played by psychiatry both in the foundation of the Netherlands Society of Psychiatry and Neurology and in its dissolution into the two separate chambers for psychiatry and neurology. Within the medical world of the first half of the 19th century, psychiatrists in particular had a need for a form of administrative organisation that would later become known as a society of specialists. There were no specialists in branches of medicine up to around 1850. There were, however, physicians with a certain degree of proficiency in surgery, where learning and experience were the determining factors. The state of affairs in the medical field was actually one of chaos in the period after the French domination; the practice of science still left much to be desired. Medicine was practiced only to a very limited extent by *medicinae doctores* from the university, and otherwise by surgeons and so-called rural physicians. It was not always clear how these practitioners acquired their medical knowledge.

Although no element of specialisation emerged in the medical world, a distinction was drawn between illnesses of the body and those of the mind. Those treating illnesses of the mind were considered to form a separate, if not a specialised, group. On the other hand, a start had been made on specialisation in those days, albeit in other countries. The primary example in this regard is Charcot (1825-1893), who, as master at the Salpêtrière in Paris, had described countless syndromes: heart, lung and kidney diseases, hysteria, the working of hypnosis, as well as a series of ailments of the central and peripheral nervous systems. Assistants of the 'internist/neurologist' Charcot included, among others, the psychiatrists Freud and Janet. In view of the fact that, in the final analysis, all organ systems are subordinated to the central nervous system, and disorders of this system had been found in a number of mental illnesses, there was an expectation that what could be called neuropsychiatry would grow into one of the first independent specialisms.

In fact, two systems were encountered in the human biological substrate:

1 a biosomatic system with organs for digestion, blood supply and muscle function, all subordinated to and regulated by the nervous system;
2 a system of mental and emotional activities with the faculty of consciousness, all regulated by the nervous system.

Whereas the matters mentioned under 1 were the concern of all medical practitioners, the matters mentioned under 2 were the realm of the doctors for nervous and mental illnesses.

One of the latter was the psychiatrist J. N. Ramaer (1817-1887), who succeeded in bringing about the formation of a society of medicine, which was founded in 1849 with Ramaer as secretary. This Royal Netherlands Society for the Promotion of Medicine (KNMG), a broad foundation for national public health, embarked on an improvement of medical training. The important point here is that it was a psychiatrist who gave rise to this general institution for all medical practitioners, which says a lot about the position of the psychiatrist in the mid 19th century.

A number of years later, the same Ramaer took a second initiative with the foundation of a Netherlands Society for Psychiatry. Ramaer took the role of chairman at its foundation in 1871. The objectives of the Society were as follows:

- the promotion of contact between psychiatrists;
- publishing the results of psychiatric research in the Netherlands;
- the dissemination of psychiatric knowledge;
- upholding the interests and rights of Dutch medical practitioners whose primary discipline is psychiatry;
- representing the interests of the insane in the widest sense of the word.

As early as 1884 the Society had arranged for the government to enact state supervision on the mental health system. Neurology was included in the title of the society in 1895. This Netherlands Society of Psychiatry and Neurology is the oldest society of specialists in the Netherlands. With respect to the name, it may be stated that there was no clear dividing line between psychiatry and neurology. In fact there was a single discipline of neuropsychiatry. The issue was often one of the anatomy of the central nervous system in relation to certain symptoms of illness.

The first reader in psychiatry (1885) was the true neuro-anatomist Cornelis Winkler (1855-1941), who gave his inaugural speech at the Willem Arntsz Huis (an asylum for the insane in Utrecht), under the title: *Psychopathology as Brain Pathology surrounded by the Clinical Sciences*. The first chair of psychiatry in the Netherlands was created almost 20 years later, and was occupied by the aforementioned reader of psychiatry. For an impression of education in psychiatry, take note of what Winkler wrote in his booklet *Recollections of Winkler*. According to Winkler, representatives of a Christian political system in the country had been endeavouring for some time to gain control of the nursing of the insane. They had founded the Vrije Universiteit in Amsterdam with a faculty of medicine, originally with only one professor, the psychiatrist L. Bouman (1869-1936). In fact, this professor was the first in the Netherlands to have his own training clinic at his disposal. When later the municipal university opened a psychiatric clinic in the hospital known as the Wilhelminagasthuis, it was a foregone conclusion that the state universities would also have their own training clinics.

The mental institution Endegeest was founded in Leiden as a psychiatric clinic under G. Jelgersma (1859-1942), who accepted his office in 1899 with a speech on psychology and psychopathology. There were but few, said Winkler, to have so many original thoughts regarding the anatomy and physiology of the brain as this gifted psychiatrist Jelgersma. In Winkler's opinion, he and the anatomist L. Bolk (1866-1930) had achieved immortality through their studies of the cerebellum, whereas Jelgersma's textbook on psychiatry could also be considered as one of the best.

The above clearly shows that in the scientific Netherlands around the turn of the century, there was only one discipline, in which, depending on the researcher, it was possible to distinguish in varying degrees between neuro-anatomy, physiology, psychopathology and sometimes also sociology. Although a clear dividing line between psychiatry and neurology was still absent, certain distinguishing features did start to manifest themselves, which was the reason in 1895, as we have seen, for the word neurology to be explicitly included in the name of the Society. If we look at the content of scientific lectures and publications we see that neurological and psychiatric subjects both appeared under the heading of psychiatry. It was very common for typically neurological and neurophysiological issues to be the subject of research of a reader in psychiatry such as Winkler, or a professor of psychiatry such as Jelgersma, while the latter, by virtue of his office, actually also wrote a textbook for psychiatry. In other words, it was not a matter of two specialisms, but of a dual specialism, which was concerned with the central and peripheral nervous systems to the extent that they were involved in illnesses of the mind and body. It was the specialism in which the practitioners for nervous and mental illnesses, the neurologists or neurologist-psychiatrists, were trained. A dual specialism it may have been, but it was a dual specialism in motion as a result of a constant differentiation in both the neurological and psychiatric directions. We will present a number of examples typical of this process of development.

Specialists are professionals who set out to know ever more about an ever smaller part of their profession. The expansion of this discipline could be determined by anatomical boundaries: the gastro-intestinal tract, heart, blood, joints, skin, etc.; by the nature of the functional disorder: epilepsy, immunity disorders, endocrine disorders, etc.; by treatment method: vascular surgery, neurosurgery, anaesthesiology, etc.; or by research techniques such as radiology, nuclear medicine, electromyography, laboratory techniques, neuropathology, etc. Ever-smaller parts of the biological research substrate are being subjected to an ever-larger number of diagnostics and therapeutics: this can be seen as the natural progress of specialisation. It goes without saying that, within the framework of this progress, countless scientists outside medical practice would participate in working groups and scientific societies that arose alongside the professional association of psychiatrists and neurologists.

For instance, a number of scientific societies were founded after the formation of the two departments (psychiatry and neurology), both before and after 1962, with the common objective of being a society in which disciplines other than psychiatry and/or neurology were to have equivalent significance and which would accept other professionals (whether or not specialists) as well as medical practitioners as members. The number of such societies was not inconsiderable, and the list below is by no means complete:

- the Netherlands Epilepsy Society;
- the Netherlands Society of Psychoanalysis
- the Netherlands Society for Psychiatrists in Employment
- the Netherlands Association of Psychoanalysis;
- the Netherlands Society of Medical Sexology;
- the Netherlands Aphasia Foundation;
- the Interdisciplinary Association of Biological Psychiatry;
- the Netherlands Society of Medical Hypnosis;
- the Netherlands Society of Child Neurology;
- the Netherlands Society of EEG and Clinical Neurophysiology;
- the Netherlands Society of Neuropsychology.

Overview

As mentioned above, the Netherlands Society of Psychiatry (1871), which has been known as the Netherlands Society of Psychiatry and Neurology since 1895, is the oldest academic specialist society in the Netherlands. At various times during its existence, it has undergone minor or major changes in its organisation. Structural changes were brought about not only as the result of pressure from its own members, but also at the instigation of the Royal Netherlands Society for the Promotion of Medicine (KNMG) or the national government. In the first half-century of its existence, the Netherlands Society of Psychiatry and Neurology succeeded in establishing chairs for psychiatry and/or neurology in Dutch universities. 1961 saw the creation of a legislative body for all medical specialisms, the Central College for the Admission and Registration of Medical Specialists (CC), which was an organ of the KNMG. The medical faculties, the ministers of education and of health, and a representative of the hospitals were also involved in the decision-making process of the CC. No specialist society whatever is represented in the CC, whereas they are represented in the executive body of the CC, the Specialists Registration Committee (SRC).

Major structural changes were imposed on the Netherlands Society of Psychiatry and Neurology in 1962 with the separation of psychiatry and neurology. The two chambers had authority with respect to the promotion of science and educational issues. The Main Board continued to be the central body for all other matters. For the sake of completeness, it should be mentioned that the Social Committee was founded in 1964 (to continue the work of the committee for social affairs that started in 1947), with a chamber for independent neurologists and a chamber for neurologists in employment. This committee was the negotiating body of the society with respect to the socio-economic interests of the members with the National Specialists Society (LSV) and the National Society of Medical Practitioners in Employment (LAD), and, through these, with the health insurance funds and other bodies.

A new code of the Consilium Neuro-Psychiatricum went into effect in 1966. This consilium consisted of chambers for psychiatry and neurology and a Consilium Contractum (with representatives of both chambers) and had an advisory role towards the Main Board on all issues that had an effect on training as a specialist.

The CC carried out a change in the specialisation, which was prepared by the society. This was concerned with recognition of the three separate specialisms: psychiatry, neurology, and nervous and mental illnesses (1971).

As was the case in 1871, at the birth of the Netherlands Society of Psychiatry and Neurology, psychiatrists were again the main driving force behind the complete separation in 1971. Psychiatry had become an immense discipline, which was ripe for further differentiation. It goes without saying that this was equally applicable to neurology. As a result, two new academic specialist societies were formed in 1974, one of which was the Netherlands Society of Neurology.

In view of the fact that initially much remained unchanged in the new society, we present below a family tree showing the branches of the organisation as they had grown until the new tree was planted. We will discuss the way in which this relates to neurology in the Netherlands until 2000 in the description of the new society that follows.

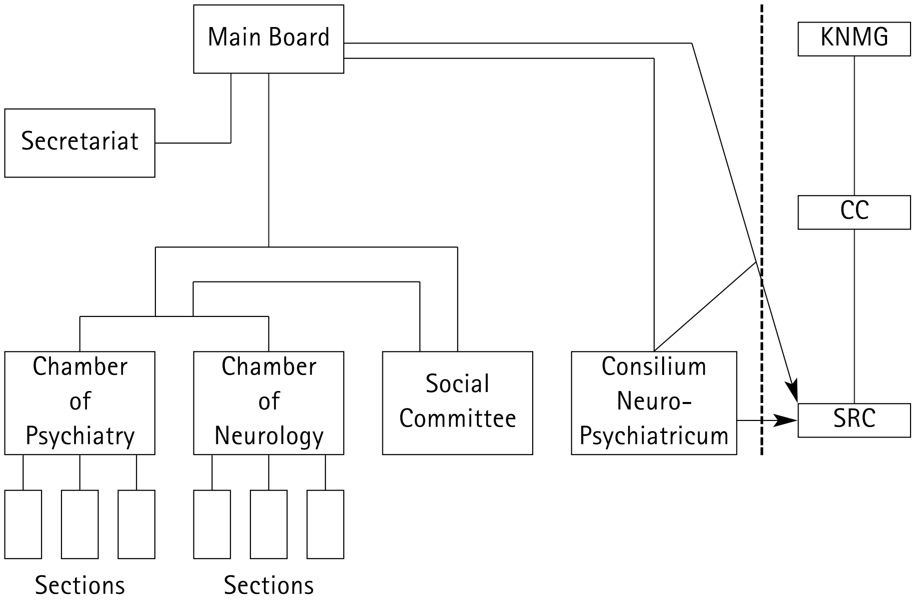

Figure 1. The branches of the organisation.

THE ORGANISATION OF THE NETHERLANDS SOCIETY OF NEUROLOGY 1980 – 2000[1]

The Netherlands Society of Neurology has been an independent organisation since 1 January 1974. The society is managed by the Board, which is elected at the annual general meeting.

The board is assisted and advised by a number of advisory organs. The oldest and one of the most important organs is the Consilium Neurologicum.

Since the early nineties the Consilium has comprised teachers from Neurology A Studies, a representative of B Studies, and an observer from the teaching clinics for Clinical Neurophysiology.

The Consilium draws up the training requirements and submits them as recommendations to the board of the society. The board then presents the requirements to the members at the annual general meeting, and, following approval by the meeting, they are submitted to the Central Board and the Medical Specialists Registration Committee (MSRC). The requirements take effect following approval by this body.

The Central Board of Medical Specialists, an organ assembled by the KNMG from representatives of the teaching hospitals and non-teaching hospitals, decides on proposals received from the consilia of the various societies of medical specialisms with respect to the training requirements, the execution of which will be monitored by the MSRC. The proposal for training requirements, as formulated by the Consilium, is submitted for further execution to the board of the society, which submits it for approval to the annual general meeting.

Another committee that has been important since the eighties in this regard is the Neurology Training Regulation Committee (CRON). The committee determines the number of junior doctors for each training institute in the Netherlands on the basis of a gentleman's agreement.

The Professional Practice Committee (CBU) advises the board of the Neurology Society on the social and financial aspects of the practice of the profession of neurologist in the Netherlands. This has had significant consequences for neurologists, particularly in recent years.

A committee formed in the eighties, the Quality Improvement Committee, advises the board on various quality aspects of the practice of the neurology profession. The committee comprises a number of subcommittees, as follows:

- Accreditation Committee: This committee determines which congresses, supplementary training and refresher courses are to be eligible for the necessary 'points' that enable a registered neurologist to renew his registration after a period of 5 years.
- Guidelines Committee: This committee assembles committees that make proposals regarding the diagnostics and treatment of certain syndromes to the Quality Committee and ultimately to the Board of the Society, which submits the proposals to the annual general meeting for approval.
- Inspection committee: This committee carries out visits and conducts assessments on site on the quality of medical treatment of the local neurological partnerships.

Another committee formed in the eighties is the Postgraduate Training Committee. This committee sets up at least two postgraduate training courses each year to put neurologists in the Netherlands in a position to enhance or refresh their knowledge. These courses, since 1999 called 'Biemond courses', also form part of the training for junior doctors.

A committee that works in close collaboration with the postgraduate training committee is the Appraisal Committee. Once or twice each year, this committee organises an assessment of all registered neurologists and junior doctors in training, in relation to general neurological subjects, and specifically to courses organised in the past year by the Postgraduate Training Committee.

In addition to these advisory bodies that concentrate on the content or execution of the profession, the board is also supported by a number of other committees, as follows:

- the PR and Public Information Committee;
- the Neurology Internet Group;
- the Neurology Scientific Research Committee;
- the Disability Committee;
- the Neurology Coding System Committee

Internationally, the Dutch Society is a member of the World Federation of Neurology and of the Union Européenne des Médecins Spécialistes (UEMS). The latter sets out to harmonise the training of neurologists in the European Union. Finally, the society is affiliated with the European Federation of Neurology, which organises annual scientific congresses and publishes an official journal, *The European Journal of Neurology*.

The Netherlands Society of Neurology publishes a scientific journal jointly with the Netherlands Neurosurgery Society and the Flemish Society of Neurologists, under the title *Clinical Neurology and Neurosurgery*.

The Society also publishes a non-academic informative journal, *The Neurologist*.

The Netherlands Society of Neurology is represented on various committees at a national level:

- the Central Supervisory Body for Peer Assessment (CBO);
- the Order of Medical Specialists;
- the Plenary Council for Science, Training and Quality of the Order of Medical Specialists;
- the Quality Platform of the Order of Medical Specialists;
- the Training Fund & Capacity Agency of the Order of Medical Specialists;
- the Epilepsy Federation;
- the Medical Advisory Board of the Parkinson Society;
- the Dutch Heart Foundation;
- the Medical Board Foundation CVA Netherlands;
- the National Society of Medical Practitioners in Employment (LAD);
- the Neurofederation of NWO;
- the Neurology - Epilepsy Consultative Body.

Finally, the Society has a number of working groups and sections:
- the Belgian-Dutch Neuromuscular Study Club;
- the Dutch Guillain-Barré Study Group;
- the History of the Neurosciences Section;
- the Interfaculty Neurology Scientific Education (IWON);
- the Netherlands Headache Society;
- the Dutch-Flemish Extrapyramidal Disorders Working Group;
- the National Botulin Working Group;
- Neuro-ophthalmology;
- Neuro-oncology;
- Impotence;
- Spinal Marrow Stimulation;
- the Pain Section;
- the Sleep Disorders Working Group;
- the Neuro-AIDS Working Group.

Note

1 We wish to express our thanks to Prof. Dr J. Troost in Maastricht for providing information on the period after 1980.

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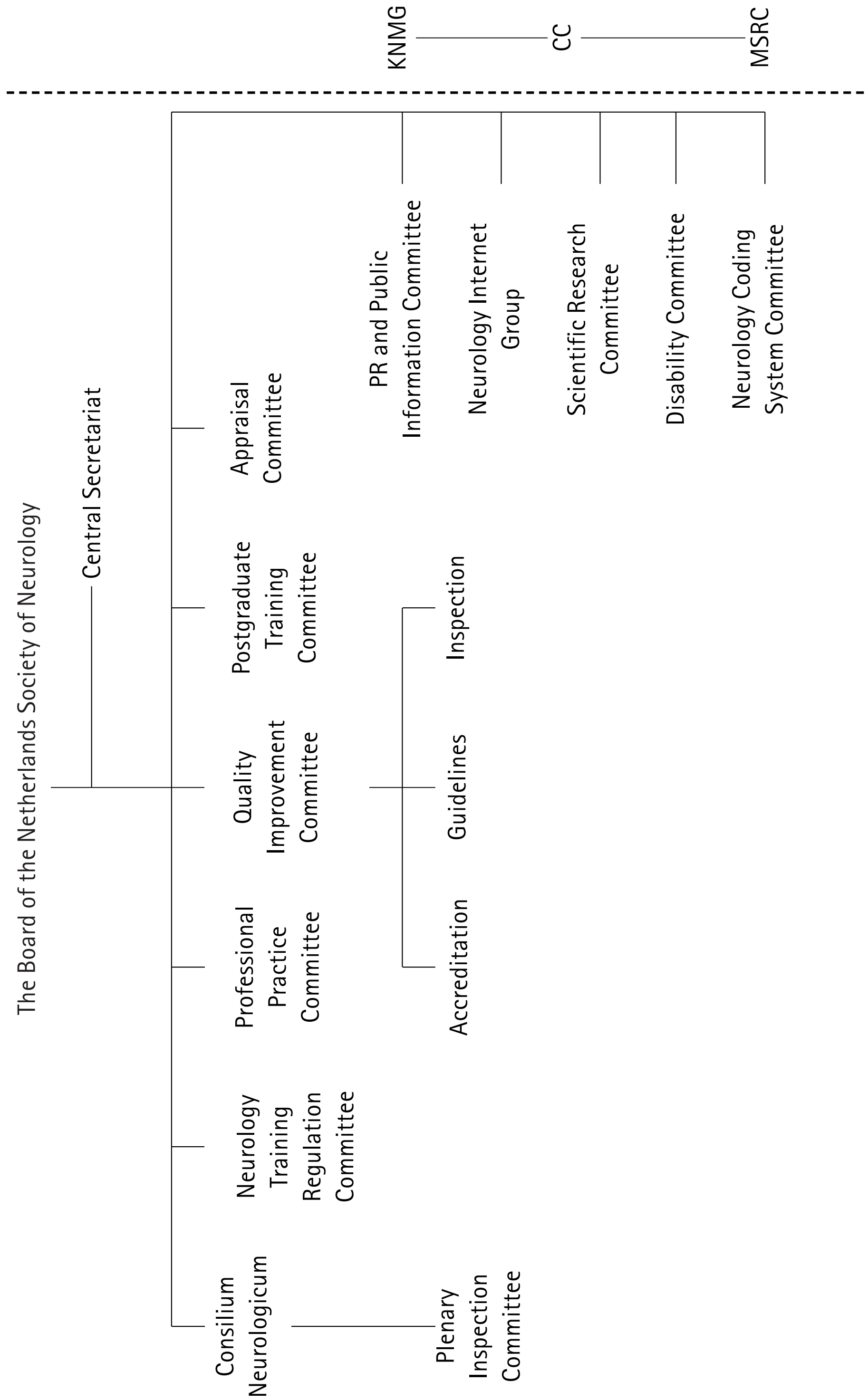

Figure 2. The board of the Netherlands Society of Neurology.

Tuition and Training

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A. Keyser

From about 1875 onwards, a neurologist was a physician who purposefully restricted himself as much as possible to the diagnosis and treatment of neurological disorders and who accumulated a specialised knowledge in this field. A young doctor interested in acquiring neurological skills joined an elderly colleague and developed his expertise in a master-fellow association. This person-centred way of training neurologists developed into a more formal training scheme with the advent of academic chairs of neurology at the various universities. The training was largely tied to the heads of the individual neurological university hospital departments. At that time chairs of (neuro-) psychiatry had been established or were under construction at the four universities. See the chapter 'Academic Chairs'.

Although it had been decided repeatedly to maintain a unified Society of Psychiatry and Neurology, the differences between these disciplines created divergent forces. The establishment of the 'Amsterdamsche Neurologen Vereniging' [Society of Amsterdam Neurologists] in 1907 was also instrumental in the formation of a strong 'Amsterdam School' within Dutch Neurology.

The Netherlands Society of Psychiatry and Neurology was the organisational body that continuously discussed and developed the training requirements for a neurologist.

By 1913 the field of psychiatry and neurology had been established at all four university medical schools, where the training in clinical psychiatry and clinical neurology was modelled.

Many neurologists wanted the subordination of neurology to psychiatry to come to an end. Some, including L.J.J. Muskens, stressed the importance of the creation of independent neurological hospital departments and the advantages of practising neurology as a specialty in its own right. Muskens already felt that the time was ripe for the two specialties to be separated.

From 1913 onwards, C.C. Nijhoff defended the idea of establishing a specialty registry in the *Netherlands Journal of Medicine*, the admittance to which should be controlled by a board of experts that had to judge the quality of the training of the specialist-to-be. This Specialist Registration Committee (SRC) should cooperate closely with the various specialty Associations as to the formulation of these specified requirements. In addition, any Scientific Association should only allow SRC-certified specialists as their members. Up to that time there were no legal or statutory regulations as to the formal requirements that had to be met in order to be acknowledged as a specialist. The Government took no initiative to introduce legislation.

As late as 1930, Nijhoff, now being president of the national Dutch Medical Association, proposed his plan to the medical community at large. The Dutch Medical Association, a private body, took the responsibility to organise what public legislation had neglected to do, and the establishment of the SRC became a fact in 1931. It would take another 30 years before a more final legal structure was established, incorporating the early private regulatory body initiated by the Dutch Medical Association into a semi-corporate legal institution, the Central College.

The newly installed SRC increased the training period of specialists from two to three years. Each scientific Society was to mandate certain deputy members to represent their specialty in the SRC. The psychiatrist H.C. Rümke was the first representative of the Netherlands Society of Psychiatry and Neurology. The SRC remained the instrument for controlling the quality of institutions entrusted with the training of specialists, and the level of instructors and trainers.

Initially, the SRC maintained a registration of all specialists on a single nationwide list in alphabetical order. Soon it was decided to create separate registers for each specialty.

From 1934, the sector in which the specialist was supposed to develop his profession was added to his name. Training took three years and the candidate-specialist had to have worked during these three years in a university department or in an affiliated clinical department of neurology elsewhere, as a resident, living within the precincts of the hospital. In those days it was a matter of self-evidence that the resident in training for a specialty was often unmarried and remained so while preparing for his future career. Women only rarely managed to finish a medical study and it was unusual to meet a female resident at the time.

During World War II the German occupier tried to change the organisation of Dutch medicine by installing a 'Nederlandsche Artsen Kamer'. A majority of Dutch physicians refused to cooperate and as a consequence the Royal Dutch Medical Association was suspended, as was the SRC and Central College. Therefore, many developments within the professional medical organisation came to a standstill through the disorganisation originating from these coercive measures that were vigorously resisted and boycotted by the Dutch physicians. The medical students were forced to undersign a so-called loyalty statement to the German occupier in order to qualify for attending lectures. Most refused to do so. Universities were closed. The 'Artsenkamer' prescribed obligatory rules, e.g., as to the duration of training for the various specialties. For example, for the specialty nervous and mental illnesses it was decided that the training would take four years, divided into two periods, i.e., two years of psychiatry and two years of neurology.

After the liberation of the Netherlands in 1945, the large number of students that had been impeded in their progress during the years of occupation had to be trained. Also a number of professionals who had continued their activities in official posts during the war period were fired. The Specialist Registration Committee resumed its duties in August 1945, J.J.G. Prick being the first representative of the Dutch Association of Neurology and Psychiatry. The following year, H.C. Rümke took over in order to continue his pre-war activities within the SRC.

In 1950, the professional training of neurologists and psychiatrists was the subject of a symposium organised by the Netherlands Society of Psychiatry and Neurology. Discussion papers were submitted by colleagues such as Prick, Ter Braak and Engelhard, some favouring the complete separation of the training of neurologists and psychiatrists, others defending the integrated status quo. The Central College consisted of parity representatives of the Specialist Societies, the medical faculties and the Ministry of Public Health and of Education. The latter, despite having only an advisory role, could veto a (intended) decision. Here, as well as in the Society, Prick from Nijmegen was a declared fighter for the integrated approach, which he defended with academic eloquence and realistic argumentation. For the time being it was decided to continue the integrated training leading to a specialty 'zenuwarts' (i.e., neuropsychiatrist).

From 1955 onwards, a proposal was discussed in the SRC concerning the inclusion in the training of neurologists and psychiatrists alike of a period of six months on the subject of 'social psychiatry'. This discussion finally led to the acceptance of this requirement in 1959. By that time, the four-year training period consisted of a composite scheme of neurology and psychiatry depending on whether one wanted to become a neurologist, a psychiatrist, or a neuropsychiatrist. The neurologist had to study neurology for $2\frac{1}{2}$ years and psychiatry for $1\frac{1}{2}$ years; the psychiatrist had to study psychiatry for $2\frac{1}{2}$ years and neurology for $1\frac{1}{2}$ years; and the neuropsychiatrist had to study both neurology and psychiatry for 2 years. The six months of social psychiatry training was to be included in the psychiatric part of the training.

Meanwhile, the centrifugal tendencies witzhin the twin specialties gained increasing momentum over the years. In 1962, the Netherlands Society of Psychiatry and Neurology established two separate departments, one for neurology and one for psychiatry, under a common main board of governors but each with their own scientific meetings and professional organisations. The progressive developments in both fields ultimately led to the splitting of the two specialties. Therefore, in 1972, the Central College decided to acknowledge both psychiatry and neurology as specialisms in their own right. This development was instrumental for the members of the Netherlands Society of Psychiatry and Neurology in splitting up the Society into two independent societies and thus The Netherlands Society of Neurology was established on January 1st 1974. This situation set the stage for the eventual training programmes in neurology as *de facto et de jure* at the end of the twentieth century.

The training for both specialties at that time was to be four years, consisting of three years of neurological training and one year of psychiatric training for neurology, and the other way around for psychiatry. Also the possibility to become neuropsychiatrist was maintained, with a five year training consisting of three years in the specialty of the trainee's choice and of two years in the twin specialism. Up to that time the training in clinical neurophysiology was only open for SRC-certified specialists who had already completed at least two years training in clinical neurology. In general this meant that only neurologists were admitted. The training in clinical neurophysiology resulted in a clause qualifying the specialist for the clinical neurophysiological diagnostic techniques. If one includes the additional year of clinical neurophysiology training, the actual duration of the training to become a neurologist at that time was therefore five years.

From 1985 onwards, the developments in the organisation of the basic training of physicians (shortening the training by one year, leading to certification as a general physician, not qualified to practice medicine independently) and the further growth in the variety of subspecialisations (childneurology, neuromuscular disorders, movement disorders, epileptology) and the necessity to become conversant with the usual techniques of neurosurgical and neuro-intensive care, meant that the training period for neurology was extended to six years, clinical neurophysiology included.

Teaching tools

The practical teaching of neurology is performed preferably in patient contact situations. However, the large number of post-war students and the restricted availability of patients frequently prevented this type of bedside teaching. Therefore, in support of the training of neurology to undergraduate medical students and interns an Interfaculty Working Group was formed in order to collect illustrative pictures of neurological disorders and in order to produce audio-visual teaching material. Neurologists from all the academic neurology departments and from the major teaching hospitals joined forces in order to obtain consensus on the best possible instructive texts and on didactic illustrations of clinical neurological cases on videocassette. H. Oosterhuis was a major impetus behind this collaborative effort. Thus a comprehensive library of video productions (N=35) concerning a wide variety of neurological disorders was created that could be called upon if it was not possible to study them in patients.

Neurology training in undergraduate and postgraduate education at the end of the twentieth century

The undergraduate teaching activity is restricted largely to the Medical Faculties of the Universities, whereas aspects of (postgraduate) training are bound to individual consultants who are usually faculty Professors of Neurology and occasionally neurologists, heading large non-university teaching hospital Departments of Neurology.

Postgraduate training

Dutch undergraduate medical education nowadays is not intended to train doctors who are ready to perform fully and independently over the whole range of medicine, surgery and obstetrics, as was formerly the case. Now the product of undergraduate education is a 'basic doctor' who is ready to start further professional training in any specialty, including the 'specialty' of general practitioner.

As to the specialty of neurology, the new M.D. has to compete for a limited number of training posts (180 for the whole country). The same clinical position with the same clinical duties is open for more undergraduates, but without the official training programme. If the candidate succeeds in obtaining a post for training in neurology, a proposal with details of the intended training programme has to be prepared by the trainee and his teacher and sent within two months to the SRC. This proposal has to be approved in advance by the national board supervising the training and the registration of specialists (SRC).

Training, organisation

The training of residents for their certification is not restricted to university neurology departments. It is also entrusted upon neurology departments in general hospitals. The Netherlands Society of Neurology set up a committee consisting of all neurologists/heads of departments who are acknowledged as trainers for the profession, i.e., the 'Consilium Neurologicum'. At the end of the last century, 15 primary, fully certified training centres for Clinical Neurology were acknowledged. In addition, eight secondary training centres were recognised where the resident can acquire practical experience in general neurology for one year. For the subject of clinical neurophysiology, the heads of 16 certified training centres form the 'Consilium Clinico-Neurophysiologicum'. Matters arising concerning the training of neurologists are discussed in periodical meetings of those committees.

The conclusions and decisions of these consilia are translated into an advice to the board of the Netherlands Society of Neurology. If proposals for changes in the training of neurologists are accepted by the board and by the general assembly of members of the Netherlands Society of Neurology, this proposal is submitted to the Central College, the official organ that makes the decision. The SRC, as the executive instrument of the CC, sees to the maintenance and faithful application of the reglementary rules that are thus created. Control of the quality of the training centres is entrusted upon a Neurological Visitation Commission, which is constituted of all members of the Consilium Neurologicum. The commission makes a judgement on the quality of the training centres and of the trainers-neurologists after having visited the centre of training, checked the neurological dossiers, the facilities, the library contents, the tuition activities and interviewed the residents in the centre. This surveillance is carried out every five years by a two-member subcommittee and a representative of the Union of Residents in Neurology, who visit the centre in question and probe its quality according to the "Prescriptions for visitations, visitation commissions and for the acknowledgement of trainers and training institutions" (SRC 1993). An important part of this visit is a confidential interview with all of the residents. A written report is produced including the points of criticism and the recommendations for improvement. If the training centre does not follow these recommendations, the institution may lose its training certification.

After passing the examination as a basic physician, the training to become a neurologist takes six years. During these years the doctor should fulfil three years in neurological patient care. Of these three years, at least 12 months should comprise outpatient care. After these three years a short training period in neurosurgery (3-6 months) is obligatory. The resident should become acquainted with all customary neurological and neuroradiological examinations and has to follow instructions in neuro-anatomy, neurophysiology and related basic sciences. He should also become familiar with the neurological aspects of pharmacology, toxicology, epidemiology and genetics. The resident has to choose a number of optional training periods (internal medicine 6-12 months maximum; and psychiatry, neuropathology, intensive care, neuroradiology, neuropsychology, and neurorehabilitation each 6 months maximum). The sum total of these training periods should not exceed 21 months. After this training period of four years and nine months, the resident follows a training of one year and three months in clinical neurophysiology. During his training period the resident has to prepare and present literature reviews and is stimulated to write one or more research papers. Preferably he should start preparing a PhD thesis.

Clinical neurophysiology

Further to the training for neurology, training for clinical neurophysiology exists. For the first three years and nine months clinical neurology is studied; in the next two years and three months clinical neurophysiology is studied (one year training in basic clinical neurophysiological techniques and fifteen months training in advanced and applied techniques).

Continuing medical education and recertification

Once he has been licensed for the specialty of neurology, the neurologist is subject to a recertification programme. Although it is obligatory, the neurologist has to apply. He should be able to demonstrate that he is actively involved in patient care for at least 16 hours a week. In addition, he should present evidence that he participates in (international) congresses on neurology and also in the bi-annual postgraduate 'Biemond Courses' organised by the Netherlands Society of Neurology. These postgraduate courses last two days and are held in a congress centre. They are intended for neurologists and they are obligatory for residents. Two months after the course an examination is organised. The exam consists of 100 questions, two thirds of them concerning the subject matter of two courses, and the remaining third on other neurological problems. Those participating in the exam receive their score as a feed back of their performance. This information is confidential and is not revealed to peers.

Postgraduate training for PhD students in neurosciences

The Dutch Universities are obliged by the government to keep an inventory of the various lines of research that are being explored by every individual department of the medical faculties. Under the leadership of the Royal Academy of Sciences, a subdivision has been created whereby each specialty distributes its main lines of research over the various universities. Thus an equilibrium is established in which any department of a certain discipline may develop its own research specialty in a particular field (discipline planning). In this way together all the university departments of a particular specialty cover the entire scientific field in question. These scientific activities are paid for by a variety of sources. The regular governmental financing supports the hard core of the medical faculty but is only sufficient for a limited amount of research projects. Therefore, additional sources are necessary. To obtain such funding a competition is organised between the various projects. The research proposals of the applicants are judged by independent boards of peer-scientists. A so-called third stream of funding comes about from gifts, specialised charities or from the pharmaceutical industry. Because Dutch Neurology is embedded in a well-organised national healthcare system, a number of multi-centre research trials are performed with the participation of the neurology departments of many general hospitals.

This type of research attracts young people who are eager to be trained as a scientist and to prepare for a PhD thesis. They earn, however, a relatively humble salary, although, in addition to performing research, they are entitled to receive theoretical education and practical instruction in the field of their activity. These additional courses are given one day a week and make heavy demands on the staff of a training institution. To solve this problem various university departments in the Netherlands with a common scientific interest have joined forces and have founded 'Medical Research Schools' , which provide a high standard of education for these postgraduate students at the national level. The residents of several institutes convene at particular universities in rotation in order to receive their scientific education. The funding for their PhD-proposals is generally limited to four years and the project should be successfully completed within this period.

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Neurological Publications by Dutch Authors

6

G.W. Bruyn and P.J. Koehler

The following pages were written on the assumption that professional literary production reflects, at least to some extent, the level of the speciality in a nation. This assumption is, of course, unproven. Is it breadth of scope or foci of interest one looks for? Is it quantity or quality; clinical work or basic neuroscience?

After due consideration of such dilemmas, the editors opted for a bird's-eye view on the admittedly arbitrary basis that Dutch neurological publications over the span of a century might mirror active professional interest, in particular because the number of neurologists (whether clinical or basic) was limited in the Netherlands, at least until the 1960s or 1970s.

A complete inventory of Dutch 'neuro-publications' constitutes a quasi-Herculean enterprise, even if one consults the compilation made by M.J. Mesdag (1922). A number of complicating factors tend to obscure the issue:

– initially, the domains of psychiatry and neurology as we know them today, were one. Specialists published works on either subject. The official (i.e., governmental) recognition for the separation of the two disciplines came as late as 1922 (in Amsterdam) and 1936 (in Utrecht) when separate chairs for the two disciplines were instituted;
– the neuropsychiatric specialists not only published in their home journal but also in journals abroad, often in the German language before World War II and thereafter in English language journals;
– in 1974, when the definitive 'divorce' of psychiatry and neurology was effected and two separate journals, one for psychiatry and one for neurology, came to replace the nearly one century old journal *Psychiatrische en Neurologische Bladen* (later *Folia*), the impact of the ISI citation-index began to spread in the Western world. The survival strategy of university departments, with an eye to staff-size, budgeting, equipment, etc., which were officially becoming dependent on the annually accumulated 'impact-points', produced an efflux of papers being submitted to journals with the highest impact-ranking (mostly of American and English signature) and concomitant anaemia of papers submitted to the Dutch home journal. Accordingly, in order to obtain a complete, exhaustive survey, one would have to ask every Dutch neuroclinician or neuroscientist for a list of his or her professional publications;
– even the last-named procedure would fall short of the goal. Because the 'impact/citation factor' automatically became tied not only to the performance of a department in gauging its quality of performance, but also to the individual neuroclinician or neuroscientist, with decisive influence on the latter's career, the

number of papers submitted boasting between four and fourteen (co-)authors soared. An author-based inventory would accordingly produce confusion by multiplicity.

Proper disentanglement of the estimated 30,000 Dutch 'neuro-publications' while keeping in mind the above-mentioned factors would take several years of research. Therefore, the editors decided to limit the scope of this chapter to the 'ontogenesis' of the journal of the Netherlands Society of Neurology, i.e., the journal *Clinical Neurology and Neurosurgery* (*CNN*). Next, a brief discussion of the *circa* 700 neurological MD theses defended at the various Dutch universities over the span of a century might contribute to an approximate sketch, if not a 'genealogy' of schools in the Dutch neurological landscape, as Kolle has done for the German domain (1970). Such a survey might also identify certain dominant foci of research. Finally, a few words are devoted to the *Handbook of Clinical Neurology* (P.J. Vinken & G.W. Bruyn 1968-2002) and neurological textbooks.

The Journal: from Bladen to Folia to CNN

The Netherlands Society of Psychiatry (NSP), founded in 1871, proved to be the cradle of neurology: members of the NSP whose fibre was more neurologically inclined and who were inspired by C. Winkler, G. Jelgersma and W.H. Cox (of the Golgi-Cox stain) saw to it that their active contribution, as a faction, to the NSP was recognised by having the name changed from NSP to Netherlands Society of Psychiatry and Neurology (NSPN). As a consequence, the Acts of the NSP, hitherto published in the *Verhandelingen van de Vereeniging voor Psychiatrie* (Discourses of the Society of Psychiatry) between 1871 and 1882, and subsequently in the *Psychiatrische Bladen* (Journal of Psychiatry) between 1882 and 1897, were now to be published in the official statutory journal of the association: *Psychiatrische en Neurologische Bladen* (PNB, Journal of Psychiatry and Neurology). G. Jelgersma (1859-1942) was the first editor (see Table I). As was the case in other countries, neurology was performed by internists as well as psychiatrists. Pieter Klazes Pel (1852-1919), professor of internal medicine in Amsterdam, for instance, published sixty papers on neurological subjects between 1878 and 1915 (Mesdag, 1922) and his residents Gerrit Waller (from 1874-1883), Constant Charles Delprat (from 1883-1893) and K.A. Wertheim Salomonson (1864-1922) did neurological consultations and had an outpatient clinic for electrotherapy.

The journal was intended to serve as a platform for original papers and exchange of thoughts among the members of the Society. Papers in Dutch, English, French or German were accepted. The PNB, it was hoped, would promote the quality of work, harmony between the members, as well as underline the social interests of the professionals. For obvious reasons, it remained a hybrid, and a rather parochial one at that, despite the many good papers it published.

As outlined recently (Koehler and Bruyn 1998), the title (PNB) remained unchallenged over a span of 51 years. Because a volume could not be produced in 1945 as a result of the battle of Arnhem followed by the winter of starvation owing to the collapse of all public transport in the occupied country which became the battle-scene between Allied and German forces, the 1948 volume carried the number 51 instead of 52. The year 1948 in this context was marked by a change of the journal's title, which was in recognition of the emancipation of the speciality neurosurgery (which was being taught at four Dutch universities at that time). In addition, the title was to reflect reconciliation between those whose ambition was to have the journal's voice heard internationally by exclusively using English as a *lingua franca,* and those who, more conservatively, feared estranging colleagues whose poor grasp of the English language might strangle their ambition to contribute to the journal. A compromise was found in the choice of the *lingua franca* of the past: Latin, producing a title as encompassing as it was cumbersome: *Folia Psychiatrica, Neurologica et Neurochirurgica Neerlandica* (FPNNN). Why the pseudo-Latin term *Neerlandica* was preferred to, for example, *Batavorum* remains a mystery. Its monstrosity must have dawned upon the NSPN's council: the title was shortened to *Psychiatria, Neurologia, Neurochirurgia* (*PNN*) in 1960 on the first page of volume 63.

The chameleon-like behaviour of the title did not stop there. When, in 1974, the NSPN split into two societies, one for psychiatry and one for neurology (the latter starting out on its autonomous life as the Netherlands Society of Neurology, NSN), the journal *PNN* continued for the NSN as *Clinical Neurology and Neurosurgery* (CNN). Because the split left the NSN with only 300-odd members of the nearly 1100 of the NSPN, and consequently with a substantially reduced readership and number of potential contributors, CNN appeared as a quarterly instead of a bi-monthly journal.

The reduced frequency of publication, the reduced membership, the exclusive use of the English language, three changes in the title (of the five) within 25 years, these symptoms taken together led to a steady decline of the journal. Because of lack of copy, apparently, another volume was dropped in 1978, so that volume 81 instead of volume 83 appeared in 1979, and the centenary volume in 1998 instead of 1996. Major additional factors in this inexorably downhill course were the low citation-impact value due to authors turning away from CNN (and causing authors to turn away!), as well as failed initiatives to merge with the neurological journals of neighbouring national societies to retain a critical readership level.

As early as 1924, the Lecturer in Neurology at Leiden, Dr. A. Gans, deplored the fact that many Dutch authors submitted their work to foreign journals. At the same meeting, B. Brouwer, President of the NSPN, suggested that PNB should merge with the *Acta Scandinavica* if the Scandinavian colleagues would agree. He stressed that PNB was scarcely read outside the Netherlands because of the language barrier. Nothing came of it, because of provincialism, conservatism, inflexibility and inertia. A similar attempt in 1986 to merge with Belgian colleagues and their *Acta Neurologica Belgica* also foundered ultimately on two issues: the boards of the Belgian and Dutch societies were unable to reach a compromise with respect to the inclusion of French-language papers submitted by francophone Belgian neurologists (Belgium being a bilingual country) and to the title of a merged Belgian/Dutch journal. Neither party wanted to relinquish its journal's title, which appeared on the Library of Congress list (a change of title could have entailed deletion from that list, although this might easily have been negotiated in Washington, D.C.). It would also have been possible to choose new title, e.g. 'Benelux Neurology'. A failed small-scale skirmish. Meanwhile, the European Community pressed its advance and, there, the journal 'European Neurology' apparently suffered no such birth-pains.

In face of the evidence, it is no wonder that the winter meeting of the NSN in the millennium-year resulted in the decision to discontinue the journal CNN at the close of 2001 (volume 103). However, plans were made to continue volume 104 in Dutch with a new title (*Tijdschrift voor Neurologie en Neurochirurgie*, *TNN*), meeting the actual needs of the NSN. When one looks through the series of volumes from 1897 onwards, one frequently comes across main papers by G. Jelgersma, J.K.A. Wertheim Salomonson, C. Winkler, J. van Deventer Szn, W.H. Cox, L. Bolk, K.H. and L. Bouman, L.J.J. Muskens, C.T. van Valkenburg, C.U. Ariëns Kappers, D.J. Hulshoff Pol, S.T. Bok, E. de Vries, H.W. Stenvers, J.G. Dusser de Barenne, L.F.C. van Erp Taalman Kip, H. Buringh Boekhoudt and G.C. Bolten in the period up to 1930. Between 1930 and 1945, contributions by leading neurologists included those by C.U. Ariëns Kappers, W.J.C. Verhaart, A. Biemond, B. Brouwer, G. Jelgersma, L. van der Horst, C. Winkler, H.W. Stenvers, C.T. van Valkenburg, V.W.D. Schenk, S.T. Bok and L.L.J. Muskens.

Table I. Editors of PNB/CNN.

1897	G. Jelgersma
1901	J.K.A. Wertheim Salomonson
1905	G.C. van Walsem
1908	J. van der Kolk
1911	C.U. Ariëns Kappers
1922	B. Brouwer
1927	H. van der Hoeven
1928	W.M. van der Scheer
1931	H.C. Rümke
1941	A. Biemond
1951	Joh. Booij
1959	A.M. Lorentz de Haas
1966	F.J. Tolsma
1971	H.M. van Praag
1974	J. Minderhoud
1990	G.W. Bruyn

After World War II and up to the late 1960s, the following prominent neurologists were the most active: A. Biemond, D. Moffie, W.J.C. Verhaart, E. de Vries, Joh. Booij, J.J.G. Prick, W.G. Sillevis Smitt, P.M. van Wulfften Palthe, C.T. van Valkenburg, V.W.D. Schenk and G. Jelgersma. The neurosurgeons, too, made their presence felt with regular contributions from Noordenbos, Verbiest, Lenshoek, Hanraets, de Grood, Luyendijk and Lambooij. Since 1974, papers by Dutch neurological protagonists, with a few exceptions, seem to have disappeared. Also, from that year onwards, one no longer finds papers from internationally known foreign neurologists whose contributions figure in the volumes of the first three quarters of the century, among whom were L. van Bogaert, R. Garcin, J. Radermecker, J. Lhermitte, M. Kennard, Sir Hugh Cairns, G. Jefferson, W. Penfield, Sir Gordon Holmes, Sir Henry Head, P. Marie, G. Schaltenbrand, Tracy Putnam, M. Bonduelle, J.J. Martin, K.J. Zülch and M. Mumenthaler.

Neurological theses

A second source of scriptorial 'production' is the MD thesis (fig. 1), usually prepared during the period of specialist training under the guidance of a 'promoter', i.e., a mentor/supervisor. The mentor must have the university's *ius promovendi* (in addition to the *venia legendi*), which is only tied to a professorship. The thesis usually takes from two to four years of part-time work, and is prepared while continuing daily duties whether clinical or in the laboratory.

The Dutch MD thesis, which has to be publicly defended during an academic hour (i.e., 45 minutes) before a jury committee, resembles the Belgian, English or Scandinavian MD thesis in terms of input of time and energy. It does not resemble the French or German MD thesis, both of which are of limited scope, depth and elaboration. It comes close to the German 'Habilitations-schrift', but differs in its consequences: by law, the 'Habilitation' must be followed by an appointment to professorship within seven years.

The reasons to include Dutch neurological theses in the discussion are:

- the thesis is a printed publication. It used to be exchanged for theses of other European universities; it reflects professional activity;
- the thesis constitutes evidence of the author's willingness to sacrifice energy, time, and often money at the altar of Lady *Scientia*. The thesis is also evidence that the author commands a gift for observation, an inquisitive mind, adheres to scientific methodology, and shows perseverance. Accordingly, one may expect subsequent publications from the author as well as well as the likelihood that he or she will follow (or return to) an academic career. Study of theses therefore holds the promise that one may sketch vectors from promoter to doctor (who eventually becomes promoter in turn), etc. These vectors may therefore reveal a 'neurogenealogy' in the Dutch neurological landscape;
- as a collection, the theses might reveal foci of interest or trends or research spearheads in the various neurological departments or even the (latent) presence of 'schools', be it that the definition of a 'school' is a complex problem and, in the modern age, has become largely devoid of significance.

A thorough study of this matter requires many years, because of a number of complicating factors briefly outlined below.

– Before the Second World War, the Netherlands had five university medical faculties (two plus the Central Brain Institute in Amsterdam, and one each in Leiden, Groningen and Utrecht). After the war, medical faculties were created in Rotterdam, Nijmegen and Maastricht. Enhanced inter-university flow of theory has only been possible therefore over the last four decades.
– In view of the rather prominent place of neuro-anatomy on the Dutch scene, it would be unfair to exclude theses of that stamp from consideration.
– Prof. J.C. Koetsier alerted the present writers to the phenomenon that theses prepared in the Valerius Kliniek (Vrije Universiteit, Amsterdam) under the responsibility of Profs. L. Bouman and L. van der Horst between 1907 and 1956 were defended (presumably because another 'promoter' was listed) at the universities of Groningen, Leiden, Utrecht and the Municipal University of Amsterdam, the reasons for such an arrangement remaining wholly obscure. A similar phenomenon confusingly occurred after World War II with some theses prepared at the medical faculty in Rotterdam, while the promoter held a chair at the university of Utrecht or with theses defended at Leiden under a promoter who held a chair at Rotterdam.
– By chance we came across a 'promoter-less' thesis from Amsterdam, which had not been published in book form, but as a large paper in the *PNB* in 1918.
– Particularly in recent decades, 'neuro'-theses have been almost always prepared under the responsibility (or, rather, the listing) of two promoters or of a promoter and a co-promoter. Perhaps this is a logical result of the complexities of modern research, nevertheless, it is often a gilding of the lily because the co-promoter's part usually remains modest if not minimal. In a numerical analysis as well as in a study of neuro-genealogical vectors this phenomenon complicates the matter unduly. One is inclined to delete co-promoterships from the material.
– A worse quandary arises when a neuroclinician and a basic neuroscientist act as promoters and one has to exclude either the one or the other to avoid duplicity.
– A final problem had to be faced: non-retrievability of pertinent data from university archives or libraries, either because data has been lost, incompletely recorded or stored carelessly. Prof. J.P.W.F. Lakke provided us with some hilarious anecdotes on this bothersome aspect.

Thanks to the full cooperation offered by (*emeritus*) professional colleagues at the various universities (hereby gratefully acknowledged), about 90 per cent of all Dutch 'neurotheses' have been traced. Having tried various methods, the most straightforward, simple and efficient approach turned out to be the initial categorisation per promoter to detect 'latent' genealogy as well as trends or foci of interest. Such an approach implies to some extent the possibility of detecting a vector pattern per university (per neurological university department, *sensu strictiori*). Of course, relatively 'young' medical faculties may be expected *a priori* not to have had sufficient time yet to reveal unequivocal neurogenealogical patterns. The analysis was done on the

Figure 1.
Promotion of David Moffie, September 1942. From left to right: Deelman (rector), Ariens (paranymph), Moffie.

assumption that the Dutch neurological 'eco-system' should readily yield the operand vectors, because of its rather limited habitat, as there were, linguistically and geographically, only five universities in the first half of the century. Therefore, a founder effect (if any) would be more readily discernible in the first half of the century than in the second. Nevertheless, the matter remains rather complicated because the definite, official separation of psychiatry and neurology occurred only in 1974 after a gestation process of fifty years. The time since 1974 is too short to detect the founding of unequivocal neurological schools. Accordingly, we only surveyed the period 1900-1975 closely, and the last quarter of the century schematically.

Municipal University, Amsterdam

Of the 52 theses guided by C. Winkler between 1898 and 1925 (39 in Amsterdam and 13 in Utrecht), 16 dealt with neuro-anatomical topics, twelve with neuropathological, nine with clinical/physiological, and nine with psychiatric. Six of these doctors became full professors/chairmen later in life, namely K.H. Bouman and B. Brouwer in Amsterdam, W.M. van der Scheer in Groningen, and J.W. Langelaan, S.T. Bok and W.J.C. Verhaart in Leiden; one became lecturer in Leiden (A. Gans).

We found two theses that had been monitored by Wertheim Salomonson, in the years 1917 and 1920. The retrieval of theses prepared under Brouwer remained incomplete; we found 21, all on neuropathological and neuro-anatomical topics, with three clinical exceptions. Four of the doctors who Brouwer had guided later assumed a professorship: A. Biemond in Amsterdam, J.J.G. Prick in Nijmegen, J.W.G. ter Braak in Rotterdam and J. Droogleever Fortuijn in Groningen.

K.H. Bouman, for whom Winkler had been both teacher and promoter (and who succeeded Winkler in Utrecht), proved strongly inclined to psychiatry; we found only a single neurological thesis (van der Heide, 1934, on Pick's disease) from his clinic during his tenure of the combined chair (1916-1923), from which the neurological part split in 1923 (Brouwer).

Brouwer's pupil, A. Biemond, during his nearly 25 year tenure, inspired at least 25 pupils to prepare their MD theses, on either clinical (neuromuscular) or neuropathological subjects. Seven of them later fulfilled leading academic positions: J. Bethlem, W.A. den Hartog Jager, J.M.B.V. de Jong and the neurosurgeon W. Noordenbos in Amsterdam, the neurosurgeon S.A. de Lange in Rotterdam, H.J.G.H. Oosterhuis in Groningen, and B.J.J. Ansink in Amsterdam also.

W.A. den Hartog Jager, who chaired neurology from 1971 to 1978 and about whom one of the most moving obituaries ever composed was written by J.M.B.V. de Jong (1993), unfortunately was not graced by fate and circumstances to transfer his scientific, experimentally inclined and clinical mind to numerous receptive MDs: we found only three theses in the year 1981, on neuropathological and clinical topics.

Of the 88(+ 7) doctors, 17(+ 2) later assumed professorates, of which nine in Amsterdam, three in Groningen, two in Rotterdam, three in Leiden, and one in Nijmegen.

Vrije Universiteit, Amsterdam

L. Bouman held the chair of Theoretical Biology, Psychiatry and Neurology from 1907-1925, then, as Winkler had done before him, moved to chair Psychiatry and Neurology at the University of Utrecht (1925-1936). We discovered no neurological theses presented by him in Amsterdam. His successor, L. van der Horst, who chaired Psychiatry (1928-1936), also took the Psychiatry Chair at the Municipal University, monitoring seven neurotheses between 1946 and 1959. One of the seven MDs later came to chair Neuropathology and Psychiatry (F.C. Stam, 1967-1988) and one the EEG Department (S.L. Visser) at the Vrije Universiteit. Therefore, their theses might appear on the lists of both universities. His successor, J.F. Folkerts, who had obtained the MD degree with a thesis on spina bifida in 1946 with the anatomist Woerdeman as promoter, chaired Neurology from 1961 to 1976 and monitored five doctorates, four of them on clinical neurophysiological methods and one on an animal experimental and histological study of sympathetic reflex dystrophy. The latter later came to chair the neurological department (J.C. Koetsier 1980-1997). F.C. Stam guided six doctorates on histochemical and neurochemical topics, one of them on a psychiatric topic. One of the six later obtained the chair of Psychiatry at the same university (W. van Tilburg). After this point in time (the 1970s), the number of neurological theses defended at the Vrije Universiteit rose markedly. It is noteworthy that all of the Vrije Universiteit's MDs stayed, as it were, 'at home', forming a sort of closed, self-fertilising eco-system. Of the eleven who gained their doctorates before 1975, two later held professorates at the same University.

Amsterdam, Central Institute for Brain Research

Established on 8 June 1909 under the auspices of the Dutch Royal Academy of Sciences, the Institute maintained close ties with the University of Amsterdam and the academic neurologists. Theses, issued from the Institute, were defended at the University. The succession of directors included C.U. Ariëns Kappers (comparative neuroanatomy) with the neurologist C.T. van Valkenburg as vice-director and Ernst de Vries, the later professor of neurology and neuropathology in Peking, Batavia and Utrecht, as assistant, the neurologist B. Brouwer, the (neuro-)anatomist S.T. Bok, the anatomist J. Ariëns Kappers, nephew of the first director and the neurobiologist Prof. D.F. Swaab, the last-named since 1978. Under Brouwer's directorate, emphasis on research was switched to neuropathology; under that of J. Ariëns Kappers to the pineal gland; and under Swaab's directorate to the hypothalamus. Because of the close academic ties and because (certainly in the first decades) the distinction between neurology and neuroanatomy/pathology was not as sharp as today, we have included the production of theses at this Institute of international repute in the present survey, even if, admittedly, they do not allow one to discern a vector-pattern in Dutch neurological 'genealogy'.

The theses prepared under C.U. Ariëns Kappers numbered ten, ranging from the lizard's brain and rabbit's thalamus to neuro-anthropometric topics. One of the MDs he had guided later held a university chair: Brummelkamp (Amsterdam, surgery). We have not counted the thesis on the poliomyelitis-epidemic in Amsterdam of 1943, because that particular thesis by A.P. van der Wey had been prepared under the guidance of B. Brouwer, whose name was printed on the frontispiece as the official promoter, but which was then covered by a label stating that Ariëns Kappers had acted as promoter, all because at the time (November 1945) Brouwer had been relieved from his chair by the authorities. The thesis monitored by Brouwer during his brief directorate (1946-9) is the one by van der Wey.

The Leiden histologist S.T. Bok guided three neurotheses while in Leiden; one of these was prepared by the later neuroanatomist H.G.J.M. Kuypers. After Bok had assumed the Directorship of the Central Brain Institute in 1953, he guided another five neurotheses. One of these authors later came to chair a department of neurophysiology (A.A. Verveen, Leiden) and two of neuroanatomy (R. Nieuwenhuys, Nijmegen, and H. van der Loos, Lausanne).

Jan Ariëns Kappers guided the work of 19 MDs, most of them focussing on the pineal gland or on the hypothalamus. One later assumed a chair of physiology (Collewijn, Rotterdam), one of neuroanatomy (D.F. Swaab, Amsterdam) and one of neurosurgery (J.P. Muizelaar, Sacramento, California).

Under Swaab's directorate, research emphasis led to the publication of 54 theses on structural, ultra-structural, neurochemical (amino acids, peptides, transmitters) and neuropathological aspects of the brain, cortex cerebri, cell-constituents and hypothalamic nuclei. Five of his students subsequently assumed leading academic positions of whom one in neurology and one in neuropathology.

The 35 neurotheses produced before 1975, led to a subsequent professorate for nine of their authors, widely spread between the old universities, Lausanne and California.

Groningen

Due to the predominant psychiatric interest of the initial ordinarii (E.D. Wiersma and W.H. van der Scheer) in Psychiatry and Neurology, holding the chair from 1903-49, the ambience for young physicians to prepare a neurological thesis appears to have been less than inspiring. For this period of nearly half a century, we found only a single thesis (on narcolepsy, 1940), guided by van der Scheer. The arrival of J. Droogleever Fortuijn (1950-73) effectuated an arousal: 23 neurological doctoral theses were passed between 1957 and 1976, seven of the authors were appointed later to a professorate: J.H.A. van der Drift (Vrije Universiteit, Amsterdam), M. de Vlieger (electroneurology, Rotterdam), S.L.H. Notermans (electroneurology, Nijmegen), J.M. Minderhoud, J.P.W.F. Lakke, S. Boonstra and E.J. Ebels (Groningen). The theses mentioned above covered a variety of neurological topics.

The period 1975-2000, beginning with the ordinariate in Neurology of J. Minderhoud will be surveyed below. The professorial issue before 1975 accordingly amounts to 7 of the 24, with positions in Groningen (four), and one each for Amsterdam, Nijmegen and Rotterdam.

Leiden

The survey of neurological theses here yields a picture that resembles somewhat the situation in Groningen: a fairly prolonged period of somnolent lethargy, one that covers an even longer time-span (1899-1975).

G. Jelgersma, chairing Psychiatry and Neurology (1899-1930) inspired two neurological and eight psychiatric theses, one on congenital cerebellar anomalies (1916) and one on the development of the CNS (1925). This confirms his biographer's statement that: "Jelgersma did not in the least encourage his pupils to write a thesis" (Carp 1943, p. 15). The theses reflected Jelgersma's life-long research focus, culminating in his unique *Atlas anatomicum cerebri humani* (1931), based on serial full-scale sections in three planes, and the similar *Atlas of the Brain of Cetacaea* (1935). Despite his neuroanatomical mastership, he created neither 'a school' nor a new generation, leaving the teaching of neurology to Ernst de Vries in 1913 (who left as Professor of Neurology and Neuropathology in 1925 for Peking, Batavia, and finally, Utrecht) and to the lecturer A. Gans (1925-45). Gans, an erudite Jew, was chronically ill from 1936 onwards, wrote a textbook on neurology, and had to go into hiding during the German occupation. As a consequence, a void lasting more than 20 years prevailed in Leiden's academic neurology.

G.G.J. Rademaker was appointed Professor of Physiology in 1928. Rademaker was a colourful figure who had been a surgical practitioner in Surabaya (1915-1920), collaborator of Magnus at Utrecht (this work led to his famous book on the red nucleus), and who was invited in 1946 to combine the physiology chair with that of neurology (1946-1957). In this hectic and confusing situation, Rademaker was apparently preoccupied with matters other than clinical neurology, in which he had no formal training. The search for theses presented by Rademaker (by Dr Hogenhuis, see chapter in this book) yielded seven; two of the seven authors later held professorates (Storm van Leeuwen and the neurosurgeon H. Verbiest, both in Utrecht); one of the MDs presented by Brouwer had done the experimental work in Rademaker's laboratory.

Only the (neuro-)histologist J. Boeke, of international renown at the time, inspired nine neurological theses in Leiden between 1912 and 1919 and five between 1923 and 1935 during his time as chair Histology in Utrecht.

While Leiden's neurology remained, as it were, at a Glasgow Coma Scale of circa 7, Rademaker's successor W.J.C. Verhaart came to chair Histology/Anatomy (1953) and Neurology (1958-1968), heading a virtual and essentially abortive creation on paper: an 'Institute of Neurological Sciences', in which were joined (at least in theory) Neuroanatomy (Verhaart), Neurology (lecturer and later professor W. Kramer), Neurosurgery (W. Luyendijk) and Neuropathology (G.Th.M. Bots). Verhaart inspired 20 neuroanatomical and one neurological thesis, reflecting his research focus, which culminated in his *Atlas on the feline brain* (improving Winkler's atlas). Of the 20 MDs Verhaart had presented, five were appointed later to leading academic positions in clinical neurology and one in neuroanatomy: Kramer (Leiden), H. van Crevel (Amsterdam), H.F.M. Busch, A. Staal and J. Voogd (Rotterdam) and A.S. de Graaf (Cape-Town). Clearly, Verhaart, from his neuroanatomical laboratory, succeeded in putting Leiden's neurology on the map again. Eight of the 38 MDs ultimately held a professorate: two in Utrecht, three in Rotterdam, one in Amsterdam, one in Leiden, and one in Cape Town.

Verhaart's successor, A. Verjaal (1970-73) did not guide any doctorates; this is explained by his advanced age at the time of appointment (62 years), the short duration of his tenure (three years) and his illness later (epilepsy).

The infertility of Leiden's clinical neurology soil changed in the last quarter of the century (*vide infra*).

Utrecht

Thirteen of the 52 theses monitored by Winkler derived from Winkler's two periods in Utrecht, i.e., 1893-6 and 1916-25; two of the MDs (Verhaart in Batavia and Leiden, and S.T. Bok in Leiden and Amsterdam) later became professors of neuroanatomy/neurology and anatomy respectively. During the periods 1900-03 and 1904-14, when Th. Ziehen and K. Heilbronner chaired the neuropsychiatric department, respectively, only one neurological thesis was apparently prepared.

From L. Bouman's period of tenure (1925-36) we retrieved eight neurotheses; one was written by B.G. Ziedses des Plantes, who later fulfilled a professorate in (neuro-)radiology, and one by W.G. Sillevis Smitt who, as Bouman's successor, was professor of neurology from 1938 to 1975 in Utrecht after the combined chair of Psychiatry and Neurology had been split. Although 'neurodegenerative' diseases was Sillevis Smitt's hobbyhorse, only one of his pupils defended a thesis on this topic, the other 14 covering a wide variety of subjects. Six of the 15 MDs ultimately held professorates: Kuiper (child psychiatry in Groningen), Bruyn in Leiden, and J. Willemse, A. Kemp, A. van Rossum and D. van der Most van Speyk in Utrecht.

Kemp succeeded Sillevis Smitt (1965 to 1982). He was mentor for five people, one of whom, F.G.I. Jennekens, came to hold a professorate in neuromuscular diseases. Most of the theses focussed on myo/neural microscopy.

W.G. Storm van Leeuwen, professor of clinical neurophysiology (1961-80) was mentor for twelve MDs, three of whom later chaired similar departments: H.A.C. Kamphuizen in Leiden, F.H. Lopes da Silva in Amsterdam and A.C. van Huffelen in Utrecht as successor to Storm. Their theses dealt with neuro-physiological problems.

Over the period 1893- 1982, 54 neurotheses were defended at the University of Utrecht. Of their authors, three went to chairs in Leiden, two in Amsterdam, one in Groningen, and eight remained at their home base.

This survey of neurological MD-theses passed at the five 'old' universities over the time-span 1893 to circa 1975/80 yields grosso modo 222 items. To this figure might be added the neurotheses passed at the Central Brain Research Institute, giving a total figure of 257. The distribution is shown in Table II. The distribution of interuniversity –'insemination'in the Dutch neuro-ecosystem is shown in Table III, which shows that intr*a*university-insemination, i.e., staying at the home base over the succession of tenures, was highest at the Vrije Universiteit and lowest at Leiden. In fact, Leiden's figure of 14 per cent may well be argued to be zero per cent if one takes into account that W. Kramer was guided by Verhaart at the University of Batavia and was called to Leiden by Verhaart after the last-named had received his Leiden appointment, thus making Leiden the most 'xenophilic' or adventurous. Be this as it may, the production of approximately 260 theses during a period that started with a mere 20 neurologists and ended with circa 320 in the ecosystem apparently reflects a motivated population of neurologists and neuroscientists, as well as the predominance of neuroanatomical topics in that period. Finally, it transpires that the 'genealogical' issue of professorates from MDs ranges from 20 to 30 per cent.

For good order, it should be recalled that the promoters of some neurotheses were not neurologists: for the MD-thesis on CNS-function (1919) by Dusser de Barenne, the Ordinarius (full professor) van Rijnberk acted as promoter, J.F. Folkerts passed his thesis on spina bifida and diplomyelia with the Ordinarius pathological anatomy Woerdeman; K. Mechelse, later heading the EEG-department at Leiden, had the Ordinarius anatomy Dankmeyer as promoter, and the epileptologist H. Meinardi at Nijmegen defended his MD-thesis on the effect of hydroxydione on the peripheral nerve under the Ordinarius physiology Duijff at Leiden (1962), while, finally, the Ordinarius physiology Ten Cate at Amsterdam guided at least two and probably many more neurotheses.

It will be clear that neuro-research in the pre-1975 period was heavily biased towards neuroanatomy and neuropathology, and that clinical problems lagged behind.

Table II. Neurothesis production between 1873 and ca. 1975. Genealogy, i.e., professorial issue, in absolute numbers (second column) and in percentages (last column).

Amsterdam Munic.U.	88	106	17	21	20
VU	18		4		
Groningen		24		7	30
Leiden		38		8	21
Utrecht		54		14	26
		222		50	23
Centr. Inst.Br.Res.		35		9	25
Total		257		59	23

Table III. Distribution of interuniversity/intrauniversity-'insemination', i.e., MDs who took university chairs; e.g., of the 17 from the Municipal University of Amsterdam 8 took a chair in Amsterdam, 3 in Groningen, 3 in Leiden, etc.

	Amsterdam	Groningen	Leiden	Utrecht	Nijmegen	Rotterdam	Cape Town	Louisiana	Sacra-mento
Munic.U. Amsterdam	8	3	3		1	2			
VU Amsterdam	4								
Groningen	1 (Free)	4			1	1			
Leiden	1 (Mun.)		1	2		3	1		
Utrecht	2 (Mun.)	1	3	8					
Centr.Inst. Br.Res.	3	1	1		1	1		1	1

A drastic change of scene occurred in the Dutch neurological landscape around 1975. A year before, the NSPN had decided to dissolve into two parties, the NSP for psychiatry and the NSN for neurology, enabling each to go its own way in the future, a definite divorce after a century of marriage. Some, optimistically or naively, may attribute the change to this decision, others, more cynically, may assert that the invigoration of Dutch neurology was brought about in spite of it and was essentially generated by latent factors (socio-economic, technological) beyond the control of the NSPN and which had already been gaining force since decades. Indeed, the formal and official recognition of the divergence between psychiatry and neurology that occurred rather abruptly at two universities as early as 1923 (Amsterdam) and 1936 (Utrecht), and at two other universities more gradually and a bit later, but still well preceding the NSPN-split (Leiden 1946 after two lectorates 1919 to 1945, and Groningen after one lectorate 1947 to 1950), pleads in favour of the view that the change had been gaining force for some time. Indeed, the government, with post-war élan, had already created two new Faculties of Medicine at which neurology was taught as an autonomous speciality (Nijmegen 1953, Rotterdam 1957) and was engaged in establishing a new university at Maastricht, an enterprise which was, as official reading went, motivated by the wish to compensate for the rising unemployment in that area due to the closure of the coal- mines... Be this as it may, the rather retarded decision of the NSPN released neurology from its kinship shackles with psychiatry and produced a boom in neurological activity. Lecturers positions were converted into professorships, subspecialties rapidly acquired sufficient critical mass for recognition of budgetary status, increases in staff numbers were scarcely without limit, and under the influence of predominant Anglo-Saxon orientation as well as the Damocletian sword of the 'impact-factor', an avalanche of neuroclinical and neuroscientific work ensued.

The abundance of neurotheses produced by the five old and three young universities over the period ± 1975-2000 compels the present authors to present only a sketch of this component of professional literary production. Only foci of research can tentatively be identified. The period, a mere quarter of a century, scarcely allows one to identify genealogical vectors, so that, with a few exceptions, we will refrain from such attempts.

The inventory covering the previous quarter-century yielded 503 MD-theses, as compared with 257 published in the preceding 82 years. It should be kept in mind that the number of colleagues holding the *ius promovendi* and monitoring MD-thesis work had risen from about 20 in the 1893-1975 era to about 60 in the 1975-2000 period. The rise is partly explained by the creation of three new medical faculties and partly by input from disciplines closely related to the clinical neurology departments. Also, we included Nijmegen in the post-1975 survey, though the Ordinarius Psychiatry and Neurology had assumed his duties as early as 1953, in addition to his appointment in the Faculty of Letters and Philosophy in 1945; three of the ten MDs he guided later held a professorate (Gabrëels and the neurosurgeon Walder in Nijmegen, and the neurosurgeon van Alphen in Amsterdam). The enhanced output then is roughly commensurate with the quasi-duplication of *ius promovendi* holders, be it that the period surveyed is three times shorter.

Short as the elapsed time may be, 36 of those who gained their doctorate have assumed a professorial position. The foci of research can be indicated as neuroimmunology || Vermeulen, myopathies || Bethlem, Marianne de Visser, motor neuron disease || de Jong, and neurometabolic disorders || Barth (Municipal University), multiple sclerosis || Koetsier, dementias || Scheltens, and neuro-oncology || Heymans (Vrije Universiteit), Craniocerebral trauma, multiple sclerosis || Minderhoud and extrapyramidal disease || Lakke (Groningen), migraine, Huntington's Chorea || Bruyn, neuro-amyloid disorders || Roos (Leiden), vascular cerebral ||

van Gijn and neuromuscular disease || Jennekens, Wokke (Utrecht), neurometabolic disease ||Gabreëls, and disorders due to DNA derangements ||Padberg (Nijmegen), neurovascular diseases, neuroimmunology and myopathies ||Staal, van de Meché, and Busch (Rotterdam) and neurovascular disease (Maastricht).

Table IV provides a synoptic view of the activity during the last quarter of the century. On observing the output of a single person with *feu sacré*, it compels one to question the merit of large staffs.

Table IV. The figures given are accurate within 5 %. For some universities, such as Rotterdam and Nijmegen, figures originating from neuroanatomical, neuropathological or physiology departments are included.
A= number of staff holding the professorates *ius promovendi*.
B = number of their MD theses promoted
C = number of (B) having acquired the *professorate*
CIBR = Central Institute of Brain Research

1893–1975				1975–2000		
A	B	C		A	B	C
6 (7)	88	17	UvA	11	57	10
4 (5)	18	4	VU	7	43	5
4	35	9	CIBR	1	52	1
3	24	7	Groningen	5	32	0
5 (6)	38	8	Leiden	5	54	8
7	54	14	Utrecht	9	68	4
			Rotterdam	10	78	4
			Nijmegen	9	95	4
			Maastricht	3	24	0
29	**257**	**59**	**Totals**	**60**	**503**	**36**

We have refrained from composing extensive genealogy schemata, because the interested reader can construct those from the data provided in the text for the period up to circa 1975. Data pertinent to the decennia following that point in time can be summarised as schematic vectors: Bethlem to Marianne de Visser, Barth in Amsterdam and W.F.M. Arts in Rotterdam; J.M.B.V. de Jong to D. Troost; van Crevel to J. Stam, van Gool, van Gijn, Evenhuis, Limburg and de Haan; Koetsier to Polman and Scheltens, J. Valk to Leenders (Groningen), van der Knaap and Heymans; Kamphuisen to Ongerboer de Visser (Amsterdam), Bruyn to Buruma, Roos, Wintzen; Peters (Utrecht), Padberg and Kremer (Nijmegen) and O.F. Brouwer (Groningen); Willemse to J. Troost (Maastricht) and O. van Nieuwenhuizen (Utrecht); van Gijn to Vermeulen (Amsterdam) and Koudstaal (Rotterdam), Kappelle (Utrecht), Jennekens to Wokke; J.J.G. Prick to Walder and Gabreëls and to van Alphen in Amsterdam; Staal to van der Lugt (Maastricht), and Voogd to Marani (Leiden) and Holstege (Groningen).

It stands to reason that the thesis survey presented above is only approximate even if fairly closely so; only a time-consuming study of source material (well-nigh impossible today, as a few universities seem to have sent old data to the shredder and have put incomplete material into 'data-bases') would allow firmer ground for conclusions. The reader is gladly left to infer his or her own conclusions from the presented information.

Handbook of Clinical Neurology

Ellison Davis (1982) has covered the history of the *Handbook*. Some background details and update may suffice here.

The idea of a handbook was born during a conversation in Vinken's study on a Saturday morning, late March 1964. Vinken and Bruyn had become friends when they shared rotating internships and residency training in the Academic Hospital, Utrecht. Both worked part-time at *Excerpta Medica*, Vinken directing the neurology section and Bruyn composing or editing abstracts of the thousands of neurological papers that appeared annually on heterogeneous topics. Rarely there was the review or single-authored monograph of the pre-war style. Classic handbooks, the monuments of the past, apparently were on their way to oblivion, replaced by an ever-growing avalanche of new and not-so-new information. The contrast of the modern motley with Oppenheim's two-volume *Handbuch*, and with Bumke and Foerster's impressive 17-volume *Handbuch* incited Vinken's musing murmur, while pointing to the piles of paper littering the floor: "Why don't we make a handbook?" A question, to which Bruyn replied "Why not, indeed?" This set Vinken in motion. He approached Biemond who, endorsing the idea, contacted Garcin and Macdonald Critchley who, within a few weeks obtained full support from Adams, van Bogaert, de Jong, Refsum, and Zülch (see fig. 2).

These neurological coryphaei constituted the editorial board of a handbook, which, before its had even come off the presses, was to become their mausoleum. Their support persuaded the directors of the North-Holland Publishing Company, Messrs. J. Frank and E. van Tongeren, to act as publishers and guarantee the investment of a considerable amount of risk capital.

The handbook was initially conceived as a series of about 30 volumes, forming a mosaic of nosologically defined categories of diseases, each chapter (review) to be written by an acknowledged expert. The language was to be English; the texts contributed by non-English speakers were to be translated. In this way, the reader of a chapter would be fully informed on any topic within half an hour, and be spared the endless toil of requesting and collecting source material from libraries. The first volume appeared in 1968.

In the course of time, circa 1300 authors from all over the world gave their time and energy to compose the circa 800 chapters of the initial series of 45 volumes. The volume editors and chief editors had to read every chapter four times: at the manuscript, revision, galley proof, and page proof stages. The administrative substructure mushroomed to the extent that an executive editor became indispensable: Mr. Ellison Davis, without whose meticulous accuracy and 'Queen's English' the venture would have suffered even more setbacks than it actually did. As more and more volumes appeared, the integrative indexing process of key words, see- and cross- references grew into a 17-stage procedure controlled by Mrs. W. van Ockenburgh.

Figure 2. Editorial Board of the Handbook of Clinical Neurology.

Neurological sciences accelerated during the period of the initial series. The electronic information revolution, of far greater impact than the Industrial Revolution of 150 years ago, the diagnostic revolution of CT- and NMR-scanning, the computerisation of the scientific (and everyday clinical) life by means of CD ROM and Internet-created source-availability, the still further reaching revolution of biomedical concepts through the armamentarium of molecular biology, necessitated a revised, updated and enlarged series, of which Volume 45 was published in 1985 and Volume 78, the last one, will appear in 2002. By that date, the *HCN* will offer 45,000 double column pages, written by some 2,300 authors, containing close to 17,000 illustrations, 5,000 tables and an index of well over 20,000 key words.

Ellison Davis (1982) wondered whether the *Handbook* in a literal sense would have any real lasting value. It will not. It will not even ever be complete, if one considers the state of fluxes certain domains such as dementia or metabolic diseases of the nervous system are in. The question, of course, is unanswerable. Does any one of us have real lasting value? Only an answer in the negative has a ring of truth.

Notwithstanding that, and fully acknowledging the major portion of non-Dutch authors who together have created the *Handbook*, one has to observe that *HCN* is a Dutch publication, originating in Dutch enterprise, with numerous Dutch-authored chapters and volume editors, and chief-edited by two Dutchmen. It is a hallmark of time, reflecting a state of neurological art, already – to some extent – in the past at the moment of writing. Perhaps with the exception of Schinz's radiology series, no other medical speciality can boast a synthesis of knowledge that remotely resembles it.

Textbooks

The two works of international repute by Jelgersma have been mentioned above. Of course, their impact does not match that of early textbooks, written in the Dutch language, such as the *General Textbook of Nervous Diseases* in two volumes by van den Broek et al. and Wertheim Salomonson et al., and the *Textbook of Nervous Diseases* in four volumes by Bouman and Brouwer. Brouwer later confessed to be unsatisfied with it himself. At the present moment, the great majority of Dutch neurologists are unaware of their existence. The one-volume *Textbook of Neurology* by A. Gans (1934) and a similar introductory one by E. Hoelen (1942) have likewise fallen into oblivion, as has Gans's monograph *Inleiding tot de Pathologie* (1950) and Posthumus Meyes's *Acute neurologie*(1950). Contrariwise, the landmark work by Ariëns Kappers on comparative neuroanatomy met international acclaim, a success recently surpassed by the sublime three-volume work on comparative neuroanatomy from the pen of R. Nieuwenhuys, who held the chair of Neuroanatomy at the University of Nijmegen (1969-1992). Last-named neuroscientist also published a book on the chemoarchitecture of the brain (1985; now, 15 years later, in need of updating) and, together with Prof. J. Voogd and C. van Huizen (1988), the best anatomical textbook on the human central nervous system for students and neurologists that has been seen in a very long time. This survey would remain incomplete without mention of A. Biemond's highly successful monographs *Diagnostiek van Hersenziekten* (1950, in English translation: *Brain Diseases* published by Elsevier) and *Ruggemergs-en periphere Zenuwziekten*, as well as the *Textbook of Neurology* by Oosterhuis, that recently saw its 14th edition. Biemond also published a book on research (1959). Certainly, Rademaker's classics of international repute, namely the *Réactions labyrinthiques et équilibre*, *De betekenis der roode kernen van het overig mesencephalon voor spiertonus, etc*., as well as his monograph *Das Stehen* (books which earned him among the students the nickname 'Prince of the Red Nucleus') proudly joined the series of prominent Dutch neuro-publications. Within this frame, the hefty monographs by the brilliant, controversial, Amsterdam neurologist L.J.J. Muskens *The Epilepsies* (with a foreword by no one less than Sherrington) and *Das supravestibuläre System* still inspire today's clinical neurologists with awe. *Réactions optomotrices* by H.W. Stenvers provided a most intelligent method of neurological examination for localising cerebral lesions, unfortunately completely forgotten today because superseded by the much faster (and incomparably more expensive) CT-and NMR-scanning.

Of smaller stature are L. Bouman's monograph on 6 personal and 94 literature cases of *Diffuse Sclerosis* (1934) and A. Verjaal's *Introductory guide to examination of*

Agnosia, Aphasia and Apraxia (1950). The book on *Poliomyelitis* (1961) by Prick, Sillevis Smitt et al. never gained the recognition it deserved. The recent *Textbook of Neurology* by the collective of Dutch neurological Ordinarii is used by neuroclinicians rather than students.

Limited space compels us not to dwell on sundry monographs by other Dutch neurologists, such as Bethlem, den Hartog Jager, Verhaart, the neurophysiologist /pharmacologist Magnus with his landmark study on body-position (1924), and the anatomist Bolk who synthesised his findings into general principles.

The summary is not complete as it does not include work by the neurolinguist F. Grewel nor, for modesty's sake, some monographs composed by the authors of the present chapter. The reader can check the reference list for any omissions from oversight or ignorance for which we offer our apologies. This brief survey seems to indicate that the most creative period in Dutch neurology, as far as books go, were the years between the two World Wars.

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Neurosurgery 7

H.A.M. van Alphen

In September 1949, the late professor of neurology and psychiatry at the Catholic University Nijmegen, J.J.G. Prick, wrote a paper on teaching in psychiatry and neurology, in which he stated: "it might be true that, in the U.S.A. and also in some European countries, neurosurgery was born of general surgery; in our country, however, its obstetrician was a neurologist and it will continue to be a legitimate child of neurology." Professor Prick made his statement in response to the Dutch neurosurgeons' ambition to emancipate their specialty. Probably, he did not realise that even a legitimate child would grow to manhood and leave his parents to go his own way. This, in fact, happened in November 1952, when the *Nederlandse Vereniging van Neurochirurgen* (Netherlands Society of Neurosurgeons) was founded and since then Dutch neurosurgeons have had to look after their own professional interests.

It is undeniably due to the initiative and strong perseverance of the neurologist Bernard Brouwer, that modern neurosurgery could be established in the Netherlands in the 1920s. Brouwer, who had been appointed Professor of Neurology at the Municipal University of Amsterdam in 1923, was invited to deliver the Herter lectures on his research in neuroanatomy at the Johns Hopkins School of Medicine in Baltimore, U.S.A. in 1926. Here he became acquainted with Walter Dandy's neurosurgical activities. From Baltimore he travelled to Boston to visit the father of modern neurosurgery, Harvey Cushing. At that time, some brain surgery was also being performed in the Netherlands by general surgeons and a few neurologists. Brouwer realised, however, that their results were lagging far behind those in the U.S.A. As he aspired to raise the level of neurosurgery in the Netherlands, on returning to Amsterdam, he made a successful request to the local authorities that neurosurgical facilities should be incorporated in his own neurological department. Brouwer continued to be an ardent advocate of neurosurgery until his death in November 1949 (Brouwer 1946).

This part of history is generally considered to be the origin of neurosurgery in the Netherlands. But it is not the whole story. Even before Brouwer's initiative in 1926, and particularly during the last decade of the nineteenth century, ample attention was paid to neurosurgery in this country (Van Alphen 1993). Once neurosurgery had been officially established in Amsterdam in 1929, neurosurgical departments were initiated in several other hospitals in the Netherlands; but it was not until 1952 that the specialty gained independence. This period of the history of neurosurgery in the Netherlands, spanning 1885 to 1952, is the main subject of this chapter.

International developments in neurosurgery

Against the background of spectacular progress in medicine in both Europe and the United States of America during the second half of the nineteenth century, neurosciences also flourished and neurosurgery progressed. The operative management of skull injuries, a dire necessity particularly in wartime, had been applied from time immemorial and even fairly systematically since the early 16th century. Yet as an approach to brain surgery, trepanation was not even widely accepted in the middle of the nineteenth century. In 1848, the German surgeon Dieffenbach wrote: "For many years, I have been more afraid of performing trepanation than of the head injuries I have had to treat; in most cases it has proved to be an effective way of killing the patient." It was not long, however, before some important conditions for a safer application of trepanation could be fulfilled. After a first demonstration by the dentist William Thomas Morton in Massachusetts General Hospital in Boston in 1846, ether anaesthesia was further developed. And, as a result of Pasteur's and Koch's discoveries in the field of bacteriology, the Scottish surgeon Lister described the principles of antisepsis in 1867. Finally, in 1873, the work of the French surgeon Paul Broca and the British neurologists John Hughlings Jackson and William Gowers, among others, proved the theory of localisation of body functions in the brain. Conversely, it also became possible to localise pathological conditions in the case of disturbance of these functions. This mapping of the different centres in the brain constituted a justifiable basis for developing brain surgery. Subsequently, Gowers considered the young English surgeon, Victor Horsley (1857-1916), to be the man to embark on this new area of surgery in London. In 1886, at the National Hospital Queen Square, he performed his first operation for a brain tumour, and, one year later, he was the first to remove a spinal cord tumour. Therefore, Horsley is considered to be the first neurosurgeon in history. However, he missed the tenacity and the firmness to define this field of medicine and thus to be regarded as the founder of modern neurological surgery (Paget 1919, Van Alphen 1999).

An analogous situation was seen in other European countries at the end of the nineteenth century, where general surgeons, including A. Chipeau and G. Marion in France, W. Macewen in Scotland, F. Krause in Germany and Th. Kocher in Switzerland, carried out many neurosurgical procedures, but in the end lacked the courage and drive to make this work their exclusive specialty (Thorwald 1990).

The developments in the USA were totally different, thanks to the inspiring dedication of a few visionary men, one of them being Harvey Cushing (1869-1939). After he had finished medical school at Harvard in Boston in 1896, he was summoned by William Halsted to Baltimore to train as a general surgeon. Here, Cushing soon developed a close friendship with William Osler, who urged him to apply himself to the surgical management of disorders of the nervous system. And so, from the beginning of 1898, Cushing started to focus on the pathology of the nervous system and trained himself as a neurosurgeon. Ever since, Harvey Cushing has become regarded as the real founder of modern neurosurgery thanks to his single-minded persistence and to his willingness to formulate his objectives again and again (Fulton 1946, Thomson 1950).

Prologue in the Netherlands

*Figure 1.
Dr. C. Winkler in the days of his appointment as university lecturer in Utrecht in 1885.*

In 1885, Cornelis Winkler (1855-1941, Fig. 1) was appointed Lector of Psychiatry at the State University of Utrecht. Under the influence of colleagues such as Meynert, Von Gudden and Flechsig, he developed a fascination for clinical and experimental neuro-anatomy and the organic aspects of neurology and psychiatry. In his opinion, neurology and psychiatry had to be taught by one and the same person and he aimed to practise psychiatry on a neurological basis. A major problem was that he did not have sufficient space at his disposal for an inpatient ward in the university hospital. He had to give his lectures in a small room in the Mental Hospital in Utrecht. The head of the department of internal medicine, Prof. Talma, allowed him to select a number of neurological patients from his outpatient clinic for instruction. In addition to this, Winkler carried out his clinical work in the Utrecht Deaconess Hospital. From the time of his appointment as lector he was under the spell of the work of Victor Horsley. As a result, Winkler decided also to focus on brain surgery. On this subject, he himself wrote: "The opportunity to intervene surgically in specific neurological cases was quite favourable in Utrecht, because my friend and fellow student Guldenarm practised surgery there, and he was technically a most talented person. He operated neatly and I did not hesitate to make an attempt to remove brain tumours with his help" (1947).

Jan Anton Guldenarm (1852-1905, Fig. 2) was born in Engwierum, Friesland in 1852. He completed medical school in 1881, underwent his surgical training with Prof. Van Goudoever in Utrecht and was then appointed surgeon at the Deaconess Hospital, Utrecht. One year later, Winkler started his clinical neurological work in the same hospital. Together, they acquired some, be it disappointing, experiences with brain abscesses. In November 1889, they operated on their first patient suffering from a brain tumor: an "angio-sarcoma in the left gyrus frontalis superior, lobulus paracentralis and the top of the gyrus centralis anterior." The patient, "a 54-year-old former infantry captain, who rarely, if ever, drank spirits, but who certainly enjoyed a glass of burgundy and loved having a good meal, after which strong cigars were smoked often to excess," died three weeks after surgery. Neither were their subsequent attempts full of glory, but "nevertheless the cured cases urged us to continue on the chosen path and, if there was any chance of success, to prefer surgical intervention to a course of arsenic or bromide, which we knew would in no way relieve the

Figure 2.
Dr. J.A. Guldenarm, surgeon in the Utrecht Deaconesses' Hospital and the Rotterdam Coolsingel Hospital, and the first Dutch surgeon applying himself to neurosurgery in the last decade of the 19th century.

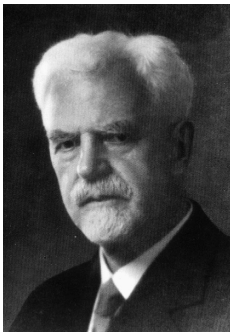


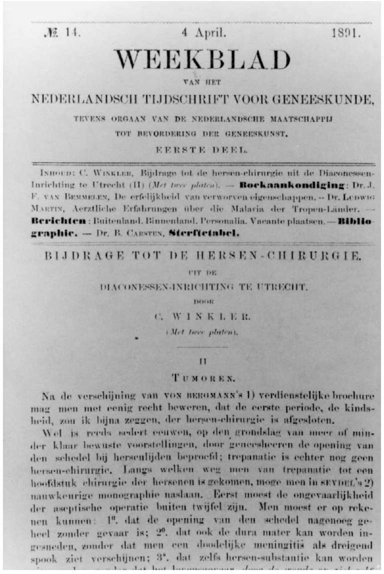
Figure 3.
Dr. Anton Freiherr von Eiselsberg, professor of surgery in the State University in Utrecht, September 1893 till January 1896.

patients' longlasting suffering" (Winkler 1891). In this way, Guldenarm, with the help of Winkler, became the first Dutch surgeon devoted to neurosurgery.

Guldenarm and Winkler thoroughly documented and revised all patient data. In 1890, they published their experiences with brain abscesses in the *Nederlandsch Tijdschrift voor Geneeskunde,* followed in 1891 by a detailed paper by Winkler on surgical treatment of brain tumours (Fig. 4), and, again together with Guldenarm, an article on head injuries. In 1892, Winkler wrote a comprehensive paper in the same journal, in which he described a method of calculating the optimal site for trephination, later known as 'Winkler's triangulation method', and in 1893 a paper on syphilitic brain tumours. In 1895, he published an essay, *On Brain Surgery,* in *De Gids*.

Winkler also had the ability to enthuse his students about this sort of work and, as a result, the first neurosurgical thesis *Operative treatment of brain tumours* by R.S. Hermanides was published as early as November 1894 (Fig. 5). In the discussion a plea was made in favour of surgical treatment of brain tumours. One of the statements ran: "For skull resection the use of a saw is preferable to that of hammer and chisel." Hermanides continued his interest in the subject (1895).

Brain surgery also flourished in the Utrecht University Hospital. This was probably due in part to the Austrian surgeon, Anton Freiherr von Eiselsberg (1860-1939, Fig. 3), who was appointed Professor of Surgery at the Utrecht University in September 1893. Prior to his surgical training with Billroth in Vienna, he spent six months in the Salpêtrière in Paris, where he attended J.-M. Charcot's lectures. Back in Vienna, he operated for trigemina neuralgia and a skull base tumour. In Utrecht, together with Winkler, who had been appointed Professor of Psychiatry in April 1893, he operated on a patient with a left frontal brain tumour on 28th April 1894. Von Eiselsberg had, like Winkler, problems with the accommodation of his department in the University Hospital. Several promises had been made on his appointment and together with Winkler he struggled to get them fulfilled; but all their efforts were in vain. When he was offered a position in Köningsberg, Germany, he accepted it and left Utrecht in January 1896. Yet, he wrote later: "I must say that I was completely happy and satisfied during the $2\frac{1}{2}$ years of my activities in Utrecht," In April 1901 he was appointed Professor of Surgery at the University of Vienna, where he continued to operate on many patients for brain tumours (Von Eiselsberg 1913,1938; Pendl 2002).


№. 14. 4 April. 1891.

WEEKBLAD

VAN HET

NEDERLANDSCH TIJDSCHRIFT VOOR GENEESKUNDE,

TEVENS ORGAAN VAN DE NEDERLANDSCHE MAATSCHAPPIJ TOT BEVORDERING DER GENEESKUNST.

EERSTE DEEL.

INHOUD: C. WINKLER, Bijdrage tot de hersen-chirurgie uit de Diaconessen-Inrichting te Utrecht (II) (*Met twee platen*). — **Boekaankondiging**: Dr. J. F. VAN BEMMELEN, De erfelijkheid van verworven eigenschappen. — Dr. LUDWIG MARTIN, Aerztliche Erfahrungen über die Malaria der Tropen-Länder. — **Berichten**: Buitenland. Binnenland. Personalia. Vacante plaatsen. — **Bibliographie.** — Dr. B. CARSTEN, **Sterftetabel.**

BIJDRAGE TOT DE HERSEN-CHIRURGIE.

UIT DE

DIACONESSEN-INRICHTING TE UTRECHT.

DOOR

C. WINKLER.

(*Met twee platen*).

II

TUMOREN.

Na de verschijning van VON BERGMANN's 1) verdienstelijke brochure mag men met eenig recht beweren, dat de eerste periode, de kindsheid, zou ik bijna zeggen, der hersen-chirurgie is afgesloten.

Wel is reeds sedert eeuwen, op den grondslag van meer of minder klaar bewuste voorstellingen, door geneesheeren de opening van den schedel bij hersenlijden beproefd; trepanatie is echter nog geen hersen-chirurgie. Langs welken weg men van trepanatie tot een hoofdstuk chirurgie der hersenen is gekomen, moge men in SEYDEL's 2) nauwkeurige monographie naslaan. Eerst moest de ongevaarlijkheid der aseptische operatie buiten twijfel zijn. Men moest er op rekenen kunnen: 1°. dat de opening van den schedel nagenoeg geheel zonder gevaar is; 2°. dat ook de dura mater kan worden ingesneden, zonder dat men een doodelijke meningitis als dreigend spook ziet verschijnen; 3°. dat zelfs hersen-substantie kan worden

Figure 4.
The first paper on the surgical treatment of brain tumours from Dr. C. Winkler.

After Von Eiselsberg's departure, Winkler also decided to leave Utrecht. He was appointed Professor of Psychiatry and Neurology at the Municipal University of Amsterdam in September 1896.

Thereafter, brain surgery in Utrecht collapsed. Guldenarm was appointed as surgeon at the Coolsingelziekenhuis in Rotterdam starting on 1st October 1896, on the recommendation of the Amsterdam Professor of Surgery, J.A. Korteweg, who, like Winkler, admired his surgical skills, and of the Utrecht Professor of Pathology, C.A. Pekelharing. In Rotterdam, Guldenarm put great effort into reorganising the department of surgery and improving the nursing school. He also continued his neurosurgical work. In the years 1897-1898 he performed 18 trepanations and three intracranial resections of the trigeminal nerve, according to a technique described by Fedor Krause some years previously. He trephined with the use of a modern electric drill and saw. He also performed the first diagnostic lumbar punctures in the Coolsingelziekenhuis. On 1st March 1899 he handed in his resignation because of a screaming row with the medical director concerning the organisation of the hospital board. With this, a promising (neuro-)surgical career ended prematurely (Van Lieburg 1986).

Winkler found a good breeding ground with respect to brain surgery in Amsterdam. In the Binnengasthuis, one of the two professors of internal medicine, P.K. Pel, was favourably inclined to neurology. His assistant, C.C. Delprat (the future historian of the *Nederlandsch Tijdschrift voor Geneeskunde*), had obtained, for the first time, a neurological outpatient clinic as a part of the internal clinic in the Binnengasthuis. He became lecturer of neurology in 1886. Once J.K.A. Wertheim Salomonson had established himself in neurological practice in Amsterdam as an associate of Prof. Pel, the self-effacing Delprat stood down and turned his outpatient clinic over to Wertheim in 1893.

Wertheim, a highly gifted man, was appointed to extraordinarius in neurology and electrotherapy and, after the discovery of the x-ray in 1896, in radiography. During the same period, Pel himself had admitted to and examined many neurological patients in his clinic and, judging by several case reports in Dutch and foreign journals (1894, 1897, 1899), had shown specific interest in brain tumours and brain

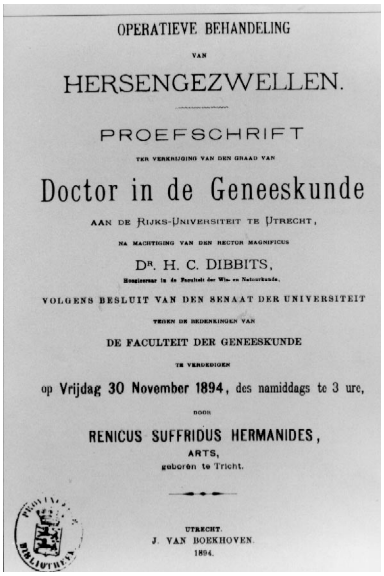

OPERATIEVE BEHANDELING
VAN
HERSENGEZWELLEN.
PROEFSCHRIFT
TER VERKRIJGING VAN DEN GRAAD VAN
Doctor in de Geneeskunde
AAN DE RIJKS-UNIVERSITEIT TE UTRECHT,
NA MACHTIGING VAN DEN RECTOR MAGNIFICUS
DR. H. C. DIBBITS,
Hoogleeraar in de Faculteit der Wis- en Natuurkunde,
VOLGENS BESLUIT VAN DEN SENAAT DER UNIVERSITEIT
TEGEN DE BEDENKINGEN VAN
DE FACULTEIT DER GENEESKUNDE
TE VERDEDIGEN
op Vrijdag 30 November 1894, des namiddags te 3 ure,
DOOR
RENICUS SUFFRIDUS HERMANIDES,
ARTS,
geboren te Tricht.
UTRECHT.
J. VAN BOEKHOVEN.
1894.

Figure 5.
Title page of the first Dutch neurosurgical doctoral thesis, written by R.S. Hermanides in Utrecht in 1894.

abscesses. Surgery in these cases was performed by Prof. Korteweg or one of his co-workers in the same hospital; histological examination was carried out by Pel's assistant J.H. Eberson.

On arrival in 1896, Winkler appointed Wertheim Salomonson as his neurological outpatient associate. Pel placed part of the internal clinic at Winkler's disposal, who, for his part, gave Wertheim the use of some beds. Winkler had already known Korteweg for a long time through Guldenarm. He also expressed much confidence in Prof. J. Rotgans, the second Professor of Surgery in Amsterdam. This atmosphere, therefore, was conducive to Winkler immediately rekindling his great interest in brain surgery in Amsterdam. With both surgeons he performed many brain operations. In 1901 he published, together with Rotgans, a review of the state of brain surgery in the Netherlands at that time (Winkler 1947), and both were co-authors of the three-volume book, edited by the French surgeon A. Chipeau: *L'État actuel de la Chirurgie Nerveuse* (1902).

Winkler also inspired young doctors to pay scientific attention to his neurosurgical results. Under his supervision H.H. Eyk published a dissertation on *Partial epilepsy and its surgical treatment* in July 1897 (Fig. 6). One of his theses was: *Doyen's drill is preferable to the trepan*. One year later, Pel's assistant, J.H. Eberson, had revised Winkler's Amsterdam material on brain tumours and published a second doctoral thesis on this subject, entitled: *On brain tumours and the results of their surgical treatment*. The supervisor in this case was Pel. A calculation shows that about ten per cent of the surgically treated brain tumours described in the international literature up to 1898 were treated in Dutch clinics. Winkler, in particular, gained an international reputation in this area and, after the turn of the century, he continued to be active in the field of neurosurgery. In 1912 he represented the Amsterdam University at the celebration of the 350th anniversary of the Royal Society in London. On this occasion he also visited Victor Horsley and attended one of his operations.

During World War I (1914-1918) Winkler went through a rough patch. Probably because of his strong orientation towards German and Austrian neurosciences, he also showed sympathy towards German politics. His attitude resulted in severe criticism from his acquaintances. Several of his assistants had to join the Dutch armed forces, which hampered the work routine in his department. And finally, as a consequence of the outbreak of the war, the plans for a new hospital and clinic faded into the background. This was probably the main reason for him to accept the invitation by the University of Utrecht to succeed Prof. K. Heilbronner, who had died from a heart attack at the outbreak of the war. An outstanding new neurological and psychiatric clinic had been built in the Utrecht University Hospital, also providing excellent research accommodation. And so Winkler made his entry as Professor of Neurology and Psychiatry in Utrecht for the second time in February 1915, where he stayed until his retirement in July 1925. During this period he worked in close cooperation with his surgical colleague Professor Laméris in the field of brain surgery. Winkler was succeeded in Amsterdam by his dedicated co-worker Wertheim Salomonson.


PARTIEELE EPILEPSIE
EN
hare heelkundige behandeling.

ACADEMISCH PROEFSCHRIFT
TER VERKRIJGING VAN DEN GRAAD VAN
Doctor in de Geneeskunde,
AAN DE UNIVERSITEIT VAN AMSTERDAM,
OP GEZAG VAN DEN RECTOR-MAGNIFICUS
Dr. C. H. KUHN,
Hoogleeraar in de Faculteit der Geneeskunde,
IN HET OPENBAAR TE VERDEDIGEN
in de Aula der Universiteit
op Woensdag den 7en Juli 1897,
des namiddags te 4 ure,
DOOR
HOYTE HENDRIK VAN EYK,
Geboren te Rotterdam.

AMSTERDAM. — J. H. & G. VAN HETEREN.
1897.

Figure 6.
Title page of H.H. van Eyk's doctoral thesis on partial epilepsy and its surgical treatment, Amsterdam (1897).

In addition to Winkler, several other neurologists and general surgeons were also interested in brain surgery during the first decades of the twentieth century, albeit on a lower and less scientific level. G. van Wayenburg, one of Winkler's neurological co-workers in Amsterdam was very surgery-minded. He regularly performed small surgical procedures, such as rib resections, preferably in the lecture hall during lunchtime. He thought this to be very instructive, but Winkler strongly disapproved and put a stop to it (Winkler 1947). Later, emulating Winkler, he became interested in the surgical treatment of brain tumours and embarked on these procedures of his own accord, in cooperation with the general surgeons C. Westerman and D. Mac Gillavry in the University Hospital. They published several case reports in Dutch medical journals (1900, 1901, 1904).

In 1899, Winkler recommended that the neurologist L.J.J. Muskens be trained in neurosurgery, because he was of the opinion that a surgeon who dedicated himself to surgery of the nervous system should also have the necessary anatomical and clinical knowledge. Muskens followed his advice and went to London to work with Victor Horsley for 20 months. Thereafter, he started to operate on his own patients in Amsterdam. He published several papers on the surgical treatment of trigeminal neuralgia, perforation of the corpus callosum in cases of hydrocephalus, and epilepsy. His results on the surgical treatment of brain tumours were disappointing. This aroused criticism from the general surgeons, who regarded Muskens to be a neurologist, while he was looked upon as a surgeon by the neurologists. Therefore, Muskens did not win high esteem for his neurosurgical work (Winkler 1947, Noordenbos 1953). Nevertheless, in a publication in 1929, he himself spoke about his experience gained in 25 years of neurosurgical practice.

In some other cities in the Netherlands, including Rotterdam and Groningen, neurosurgical procedures were performed incidentally by general surgeons, neurologists and even dentists. These activities, however, lacked a structural basis during the first three decades of the twentieth century, and the results generally fell short of expectations.

The first neurosurgical clinic in Amsterdam

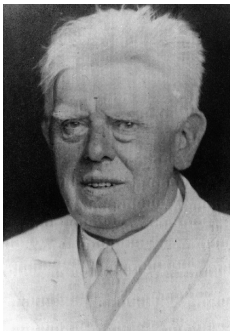


Figure 7.
Prof. Dr. B. Brouwer, neurologist in the University Hospital in Amsterdam, and spiritual father of neurosurgery in the Netherlands in the 1920s.

In Amsterdam, Wertheim Salomonson died suddenly in September 1922. In his place, Winkler's student Dr. Bernard Brouwer (1881-1949, Fig. 7) was appointed Professor of Neurology. Prof. K.H. Bouman, who until that time had been teaching neurology and psychiatry, decided to continue with psychiatry only. Brouwer had observed a gradual rise in the number of organic neurological diseases in his clinic, including disorders that required surgical treatment. Such treatment was carried out by the general surgeons Prof. O. Lanz (1865-1935) and Prof. W. Noordenbos Sr. (1875-1954), among others. However, Brouwer was of the opinion that the results were lagging behind those reported in the American literature. Contact with Dandy and Cushing during his 1926 visit to the USA resulted in Brouwer becoming an advocate of neurosurgery. He realised, however, that neurological diagnostics in Holland were not up to date, that the understanding of changes of intracranial pressure was insufficient, that haemostasis during surgery was inadequate, and that postoperative care was of great importance. He decided to put neurosurgery on a higher level. He had been offered a professorship in neurology in Baltimore with the opportunity of obtaining a new neurological clinic, but Amsterdam was very keen for him to return. Hence, Brouwer could make considerable demands in his negotiations with the city council of Amsterdam. The most important demands were that he would be allowed to create his own neurological clinic, and that it should be equipped with a modern neurosurgical unit. The city council reluctantly agreed to these terms in June 1927 (Brouwer 1946).

Brouwer realised that modern neurosurgery, as he had witnessed in the U.S.A., could only get off the ground in Amsterdam if surgeons could be found who were prepared to apply themselves undividedly to neurosurgery. In his conception, the neurologists should select the patients for surgery and should carry out the time-consuming and painstaking neurological examination. From the candidates who presented for neurosurgery, Brouwer choose Ignaz Oljenick.

Ignaz Oljenick (Fig. 8), a son of Czech-Jewish parents, was born in the Netherlands and studied medicine in Amsterdam. He was training as a general surgeon with Prof. Lanz, and had also worked in the neurological outpatient clinic with Wertheim Salomonson and Brouwer. Brouwer sent him to Boston in 1927 to be trained as a neurosurgeon by Harvey Cushing where he worked as a *voluntary graduate assistant* together with Hugh Cairns, future leading neurosurgeon in London and Oxford. Both had a hard time with Cushing. Cairns, who was an Australian veteran of World War I, later confessed that "Gallipoli and the battle of the Marne were as nothing compared with the clinical stress of a year as Cushing's neurosurgical resident" (Fulton 1946). They participated in Cushing's research as 'the principal recorders' of one of the case reports in his book: *Tumours arising from the blood vessels of the brain* (1928). Oljenick returned to Amsterdam in March 1929. Meanwhile, the neurological clinic, in the Wilhelmina Gasthuis, one of the University Hospitals in Amsterdam, was reaching completion. On September 23rd 1929 the first neurosurgical unit in the Netherlands opened its doors, and Oljenick started work as the first Dutch neurosurgeon. The clinic had 120 beds, as many as necessary being available to neurosurgical patients. Initially this was about 20 per cent, later 25 per cent of the total number. Before the clinic opened, in May 1929, Brouwer had put an advertisement in the *Nederlandsch Tijdschrift voor Geneeskunde* for a resident, to be trained as a neurosurgeon by Oljenick. Arnoud C. de Vet was selected and started his training in September 1929.

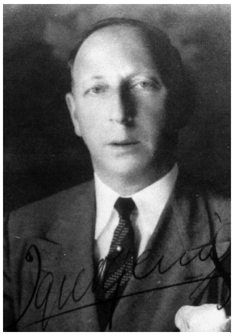


Figure 8.
Dr. I. Oljenick, first properly trained neurosurgeon in the Netherlands, who started his work in September 1929, and who had to escape the country from the German occupiers in May 1940.

Just like Cushing in Boston, Oljenick himself examined all the patients who were to be operated on very carefully together with the residents, and he kept his own clinical records. He also performed his own radiological studies and, together with Brouwer, the histological examinations of the surgical material. Soon he became well known for his efficacious antisepsis and his painstaking way of operating with good haemostasis. In a short time, his surgical results exceeded all expectations, leading to the referral of many patients from elsewhere. Oljenick was also a doubter and quite conservative with little vision of the future. He operated very slowly, which resulted in much criticism. He was hard and sometimes quite unreasonable to his co-workers. During his career in Amsterdam, Oljenick published about ten papers on subjects including the clinical significance of Parinaud's syndrome, increased intracranial pressure and the surgical treatment of extra- and intramedullary tumours (1928, 1932, 1937). On 18th October 1939 he wrote an In Memoriam to Harvey Cushing, who had died the day before. He did not write a doctoral thesis. At the end of the thirties, Oljenick also performed neurosurgical procedures in the Valeriuskliniek in Amsterdam and acted as *locum tenens* for De Vet's practice in Wassenaar during holidays.

From 1938 he trained a second future Dutch neurosurgeon, Paul M. Hoeberechts, and also supervised a few residents from abroad. On the day before Amsterdam fell to the Germans, in May 1940, he fled to England, because he was Jewish, and later went to the U.S.A. Here, he changed his name to Olninck. In New York he practised as a cosmetic surgeon and prepared expert's reports for victims of the German war (Brouwer 1946). There is no further record of his career and he was last seen by his student De Vet at the world congress of neurosurgery in New York in 1969.

The period 1929–1940

From the beginning, Brouwer proved himself a strong promotor of neurosurgery, focussing attention on its potential through numerous lectures and clinical demonstrations. Every year he reported on the numbers of patients operated upon in Amsterdam. With respect to the division of tasks between the neurologist and the neurosurgeon, as desired by Brouwer, things went less smoothly, which was understandable. During his visit to the U.S.A., Brouwer had already seen that Cushing had broken away from the actual practice in those days, namely that the surgeon was only the technical executor of the neurologist. He himself wrote about this (1946): "Cushing himself examined his patients and localized the disorders in the central nervous system, he operated meticulously and bore the responsibility for the aftercare with painstaking accuracy." It was only to be expected that Cushing's student, Oljenick, would adopt this method of working. Oljenick was indeed an excellent diagnostician. With this dualism, tension arose between neurosurgeons and neurologists. As recently as 1984, De Vet phrased the latent conflict as follows: "The first 15 to 20 years of the existence of neurosurgery in the Netherlands formed so to speak a period in which this new specialty grew and flourished. The only really serious drawback was, however, that Neurosurgery was completely subordinate to Her Majesty Neurology. (...) This was due to the fact that the neurosurgeons as meek lambs were led by neurological profundities during the first 15 years, only coming into action when the wise neurologist gave the green light." A striking example of this situation was the following: For localizing a brain tumour Oljenick applied Walter Dandy's ventriculography, but Brouwer only allowed him to do so, if the patient had papilloedema. When Oljenick also wanted to perform arteriography in Amsterdam, as described by the Portuguese neurologist Egaz Moniz in 1927, Brouwer forbade him, because he judged the risks to be too great.

In 1931, the neurologist Ed. Hoelen asked Brouwer to lend his support to the foundation of a neurosurgical department in a new neurological-neurosurgical institute still to be built in Wassenaar. In the autumn of the same year, Hoelen invited Oljenick's resident De Vet to come and work as a neurosurgeon in Wassenaar after completion of his training in Amsterdam. De Vet accepted this challenge. The institute was opened in 1936 and named St. Ursulakliniek after De Vet's first wife, who had died from a car accident three months after their marriage in February 1935.

Arnaud C. de Vet (1904-2001, Fig. 9) was born in Alkmaar and studied medicine at the Municipal University of Amsterdam. After finishing medical school in 1929, he saw Brouwer's advertisement in the *Nederlandsch Tijdschrift voor Geneeskunde*, asking for a neurosurgical resident. De Vet applied and was accepted. In September 1929 he started his training programme, consisting of one year of residency in general surgery in Rotterdam and five years in neurology and neurosurgery in Amsterdam. After finishing this training, De Vet went on a seven and a half month study tour through Europe, during which he visited the neurosurgeons Cairns in London, Olivecrona in Stockholm, Foerster in Breslau and Vincent in Paris. During this period, he finished his doctoral thesis, *On the diagnostics of the menigioma cerebri*, which he defended, after his return to Holland, on April 3rd 1936. In May thereafter, the St. Ursulakliniek was opened, and De Vet started his neurosurgical work in Wassenaar. He was praised for his careful operating technique. His special interests were the surgical treatment of meningiomas, cerebrovascular disorders and epilepsy. He also had a broad scientific interest: he presented many lectures at home and abroad and published 62 papers on quite different neurosurgical subjects, such as *The organisation of neurosurgery in the Netherlands* (1967, 1981). De Vet trained eight Dutch neurosurgeons: P. Hoeberechts (partially), P. Hanraets, who later became his associate and co-teacher, M. Weersma, A. Walder, E. Meijer, M. van Duinen, N. Lambooy and C. Tulleken. He also received several trainees from abroad, including K. Handojo from Indonesia, Radakishun from Surinam, and F.T. Merei from Hungary. He regularly visited neurosurgical congresses abroad. He worked as a neurosurgeon in the former Dutch East Indies for 9 months in 1950, and he visited many colleagues all over the world. In 1955 he was one of the founders of the World Federation of Neurosurgical Societies, in which he held several offices. De Vet retired in December 1969. He was awarded the honorary presidency of the Netherlands Society of Neurosurgeons, the honorary membership of the Netherlands Study Club for Neurosurgery and of several foreign neurosurgical societies, and the Medal of Honour of the World Federation of Neurosurgical Societies (Van Alphen 2001).

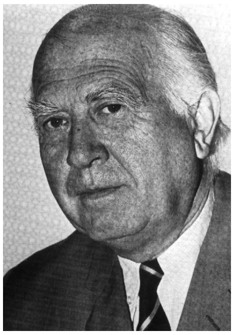


Figure 9. Dr. A.C. de Vet, trained by Oljenick and later neurosurgeon in Wassenaar.

Circa 1930, plans were made to practise neurosurgery in the University Hospital, Groningen, but this soon led to disagreement and rivalry between the general surgeons and the neurologists about who should supervise neurosurgery. Because he was unsatisfied with the situation, the Professor of Neurology, W.H. van der Scheer referred his patients to Oljenick in Amsterdam for neurosurgical treatment for the first few years. This caused great upheaval not only among the surgeons but also among the other medical specialists, who saw their patients disappear elsewhere. Therefore, in 1932, the Professor of Surgery, Michaël, sent one of his residents, F.A. Verbeek, to the United States to be trained in neurosurgery.

Figure 10.
Dr. F.A. Verbeek, neurosurgeon in Groningen from 1936 till 1958.

Ferdinand A. Verbeek (Fig. 10) was born in Veghel, the son of a family doctor. He studied medicine at the State University in Groningen. His brothers were also physicians. He trained in general surgery for two years before going to the United States in June 1932. There, he first spent a few months with Harvey Cushing in Boston, as his last foreign assistant before his retirement. Verbeek then left for Baltimore to work as a *voluntary assistant* with Walter Dandy in the Johns Hopkins Hospital. During his stay in Baltimore Verbeek married his wife Elizabeth, who was given away by Dandy (Fox 1984). He returned to Groningen in January 1935 and was appointed senior assistant in the department of general surgery. However, Verbeek, who was quite impulsive and short-tempered, got on very bad terms with the senior consultant of the department, J. Boerema. He was allowed to perform neurosurgical procedures only once or twice a week; he was not satisfied with the sterility in the operating theatre and accused Boerema of being responsible for postoperative infections. Their constant arguments and fights led to Verbeek's dismissal from the University Hospital. He moved to the Roman Catholic Hospital in Groningen on the 1st of November 1936. Initially, he had 15 beds at his disposal, which were spread all over the hospital. Another problem was, that, as a neurosurgeon at that time, he was not registered with the National Health Service and was not paid for his neurosurgical procedures. Therefore, he also had to practise general surgery. In subsequent years he equipped his own neurosurgical unit, which ultimately comprised 25 beds for adults and nine for children and babies, and a modern operating theatre. Prof. Brouwer officially opened the unit on 26th July 1941. At Prof. Prick's request, Verbeek also carried out neurosurgical procedures in the Canisius Hospital in Nijmegen once a week from 1937 onwards. Again because of frequent rows with colleagues and nuns he was dismissed in Nijmegen after a few years. Verbeek was a skilful and meticulous neurosurgeon. In the period between 1935 and 1945 he performed 1357 neurosurgical procedures. The operative mortality was 13.5 per cent, which was not bad in those days (Brouwer 1946). Verbeek did not write a doctoral thesis, and he did not train neurosurgical residents. On 20th July 1946 he wrote an In Memoriam to his teacher, Walter Dandy. His most important administrative merit was his initial impetus to the formation of the *Nederlandsche Studieclub voor Neurochirurgie* (Netherlands Study Club for Neurosurgery) in 1936 and his dedicated fulfilment of his position as secretary-treasurer until his death. During the last years of his life, Verbeek became mentally ill. He committed suicide in the psychiatric hospital Heiloo on 16th October 1958.

As we have seen above, Utrecht already had a history of neurosurgery. In the University Hospital it was particularly the general surgeon Prof. Laméris who regularly performed neurosurgical procedures. In view of the national developments, he and the Professor of Neurology and Psychiatry, L. Bouman, decided to send one of his co-workers, C. Lenshoek to Prof. Clovis Vincent in Paris to be trained in neurosurgery. Vincent had originally been a neurologist, a student of Babinski. Later, Harvey Cushing in Boston trained him in neurosurgery. Due to this neurological background, his way of working was quite different from the American school, which was based on general surgery. Vincent was, together with Thierry de Martel, the founder of neurosurgery in France.

Figure 11. Prof. Dr. C.H. Lenshoek, neurosurgeon in Utrecht, Amsterdam and Groningen, in that order, from 1936 till 1968.

C.H. Lenshoek (Fig. 11) was born in the former Dutch East Indies. He studied medicine at the State University of Utrecht and afterwards underwent a full training in general surgery with Laméris. He took his Ph.D. degree with a doctoral thesis in 1931, entitled: *Medical chemistry and surgery. Surgical treatment and reaction of blood and tissue fluids*. He left for Paris in 1933, where he spent two and a half years in neurosurgery. On his return to Utrecht in 1936, he started neurosurgical work in the University Hospital in close cooperation with the neurologists Prof. W.G. Sillevis Smitt and H.W. Stenvers. H. Verbiest, who had been sent from Leiden to Paris in 1938 to train with Clovis Vincent, but who had had to return to Holland in 1939 because of the threat of war, joined Lenshoek in Utrecht to continue his training with him. In 1940, shortly after Oljenick's escape to England and the United States, Lenshoek moved to Amsterdam to take over the position in the Wilhelmina Gasthuis with Brouwer. Verbiest went with him to finish his training until mid-1941. In Amsterdam, Lenshoek found another neurosurgical resident, P. Hoeberechts, who had trained with Oljenick as from 1938 and who left for Wassenaar in 1941. During and after the war, lumbar disc surgery became widely known thanks to Lenshoek. He also had a special interest in sympathetic surgery and the treatment of causalgia and phantom limb pain. In 1948, Lenshoek went to former Batavia, Dutch East Indies for one year to cooperate in the foundation of a new medical school. P. Hanraerts, who later went to Batavia to practise neurosurgery, reported that he found no neurosurgical equipment or facilities on his arrival in 1949 and had to arrange these. Lenshoek was appointed Professor of Neurosurgery at the State University in Groningen on 1st January 1955, which was the first neurosurgical chair in the Netherlands. His inaugural lecture bore the title: *From antithesis to synthesis in neurosurgery,* in which he urged a harmonic cooperation between the neurosurgeon, the neurologist and the general surgeon. The freethinking Lenshoek was averse to patronising people. His closest colleagues in Groningen were the general surgeon Prof. Eerland and the neurologist Prof. Droogleever Fortuyn. Lenshoek retired in 1968. His valedictory lecture read: *Some historical considerations on neurosurgery in the Netherlands*. Lenshoek was kind and charming with a modesty verging on shyness. He did not publish many papers. In Amsterdam he trained four other neurosurgeons:

W. Noordenbos, who became his associate and later successor, M.P.A.M. de Grood, who later went to Tilburg, G.J. van Hoytema (Enschede), and S.A. de Lange (Rotterdam). In Groningen he had five trainees: J.F.M. Beks, later his associate and successor, T.B. Sikkes (Verbeek's successor at the R.K.Z., Groningen), J. Dijksterhuis (Zwolle), N. Bosma (partly, Utrecht), and K.G. Go (Groningen).

Netherlands Study Club for Neurosurgery

The Netherlands had four neurosurgeons in four different locations at the end of 1936. The general surgeons were of the opinion, that, with this number, all brain tumours in the Netherlands could be surgically treated within one year, and that after that year there would no longer be any employment for the neurosurgeons. The neurosurgeons themselves also had a question mark over their future. Therefore, it was agreed that the number of neurosurgeons should not be increased for the first ten years. There were more reasons for tension and areas of friction, such as the surgeons' rivalry, the neurologists' patronising attitude, efforts to obtain their own facilities, finding sufficient space to work professionally in the different hospitals, and occasional internal competition. This was probably the main reason why Verbeek, who had had a tough start in Groningen, wrote a letter to the godfather of neu-

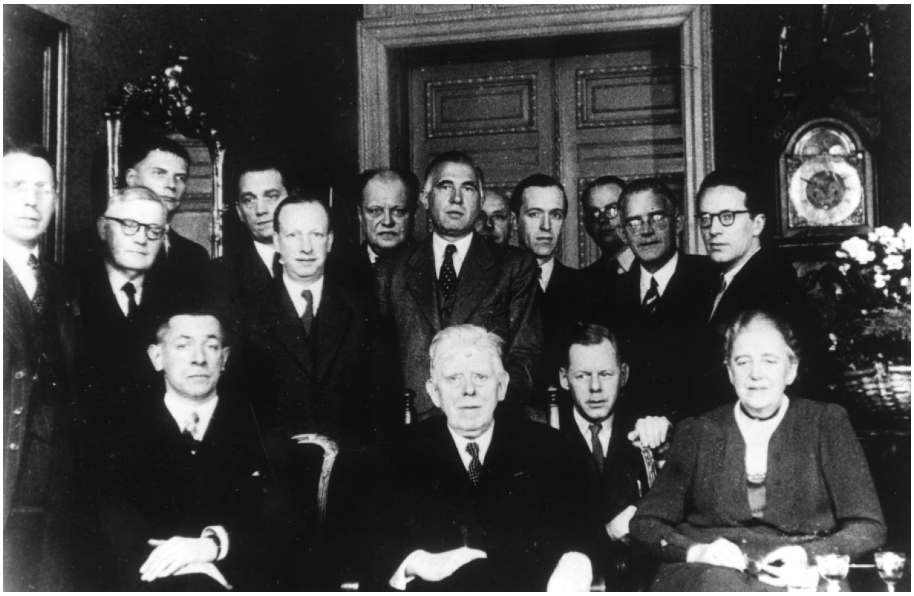


Figure 12.
Netherlands Study Club for Neurosurgery, meeting at B. Brouwer's place in 1947.
First row from left to right: F. Verbeek, B. Brouwer, W. Noordenbos, Mrs. Brouwer; behind: J. Prick, H. Stenvers, W. Sillevis Smitt, H. Verbiest, B. Ziedses des Plantes, E. Hoelen, A. de Vet, M. Weersma, P. Hoeberechts, M. de Grood, A. Biemond and P. Hanraets.

Figure 13.
Netherlands Study Club for Neurosurgery, gathering in Amsterdam 3 November 1984 at the occasion of the 100th meeting.

rosurgery, Prof. Brouwer in Amsterdam on 18th September 1936, asking for a talk. This took place in the first week of October. Verbeek asked for Brouwer's cooperation in creating regular neurosurgical meetings under his leadership. Brouwer agreed, but he deemed it undesirable to start with an official association immediately. He proposed founding a study club with a limited number of members. He invited the four neurosurgeons for a meeting in his institute on 7th November 1936, during which the *Netherlands Study Club for Neurosurgery* was officially founded. The objective was vaguely defined as the promotion of neurosurgery among its members. Brouwer and the neurosurgeons were to be ordinary members. A limited number of neurologists became associate members who had no vote. Brouwer was chosen as the lifetime president and Verbeek as secretary-treasurer. There were four meetings a year on a Saturday afternoon, held in the neurosurgical centres on a rotational basis. Attendance was compulsory. During the meetings, two clinical lectures or difficult neurosurgical cases on different subjects were to be presented by the hosts and discussed by the audience. The presentations and discussions were reported extensively by Verbeek. A business meeting was sometimes held prior to the scientific meeting, where matters of professional interest, such as training programme, registration, set-up of new neurosurgical units, fees, etc., were discussed. Although the associate members had no vote in these matters, they did not remain silent. The discussions were sometimes very sharp and offensive. Later on, the oral sessions were preceded by surgical demonstrations in the morning by the neurosurgical host, followed by a lunch in the hospital. The day was concluded with a dinner at the host's home (Fig. 12). At this stage Brouwer reviewed the scientific part of the meeting critically and made reference to those who had erred; he thanked the board of the hospital and the hosts appropriately for the instructive day, and finally requested a moment's silence for prayer. This speech is still referred to as the 'evening prayer' (De Vet 1984). It is obvious that Brouwer had a prominent and authoritative role in this study club. For example, the composition and duration of the neurosurgical training programme and the registration were subjects of discussion in 1937. Brouwer advised the Specialists' Registration Committee that the training programme should include one to three years of general surgery and at least four years of neurosurgery. He judged a purely neurological training to be unnecessary. He also felt that neurosurgery should descend from general surgery, rather than from neurology, a view with which many neurologists did not agree. Verbeek for his part was of the opinion that neurosurgeons should be registered as surgeons and not as neurologists, at least in the beginning, as long as neurosurgery was not recognised as an independent specialty. He wrote to De Vet: "I am convinced that neurosurgery has to be considered as the most difficult branch of surgery and not as the playground for the frisky neurologist of the future." In 1940 the discussion was extended to the *Nederlandsch Tijdschrift voor Geneeskunde* with a dispute between Stenvers and Verbeek on the relationship between neurology and neurosurgery. During the war these discussions abated, because everyone had other worries; but afterwards they flared up again, as we will see later.

The organisation of the meetings of the *Study Club* encountered many difficulties during wartime. Travel became more and more difficult and finally almost impossible. The German occupiers issued a prohibition order on public meetings. This was why the frequency of the meetings had to be decreased from 1939, and why no meetings at all could be organised in 1944 and 1945.

On 1st November 1949, Prof. Brouwer died "suddenly, as if hit by a thunderbolt, in the middle of his work" (Biemond 1950). He was commemorated rightly as the great pioneer and founder of modern neurosurgery in the Netherlands. This was the turning point in the course of the *Study Club*. Lenshoek, who had been vice-president since its inception, became president; Ed. Hoelen became vice-president. From then on, the president was to be succeeded by the vice-president, who was to be chosen every three years and who should be alternately a neurosurgeon and a neurologist. The frequency of the meetings was decreased to twice a year as from 1950. The surgical demonstrations prior to the meetings were abolished. After the Netherlands Society of Neurosurgeons had been founded as a proper, professional association in 1952, the neurologists became ordinary voting members of the *Study Club*. The membership was extended to two neurosurgeons and two neurologists from each centre. An associate membership could be granted to specially invited individuals, who were neither neurosurgeons nor neurologists. The senior-membership was introduced for retired members but they had no vote. The form of the meetings also changed in the course of time. The number of presentations by the hosts increased and was planned in a morning session. The reports were published in a syllabus, which was sent to the members in advance, to encourage discussion. This was held after lunchtime, and followed by the business meeting. From 1959 onwards, the members' spouses were also invited for cocktails and dinner after the meeting. The *Study Club* had become a steady club without the heated debates and sharp competition of the early years.

The hundredth meeting took place on 3rd November 1984, and was celebrated in grand fashion in De Nieuwe Kerk (The New Church) in Amsterdam. The attendance was overwhelming (Fig. 13). De Vet gave an address on his personal memories since the foundation in 1936. D. Moffie, H. Verbiest, B. Ziedses des Plantes and O. Magnus looked back on the developments in neurology and neuropathology, neurosurgery, neuroradiology and neurophysiology respectively, during this period. The dinner was held in the restaurant annexed to *De Nieuwe Kerk,* and the President, the eloquent neurologist, B. Schulte, concluded the evening with a dignified evening prayer. The fiftieth anniversary was celebrated more modestly during the meeting in Enschede on 8th November 1986, and the sixtieth exactly ten years later, again in Amsterdam.

Neurosurgery in wartime

On 10th May 1940, the German Army invaded the Netherlands. The first loss to neurosurgery in this country has already been mentioned, namely that Ignaz Oljenick fled abroad to escape from the Germans as he was Jewish. The acts of war had sometimes far-reaching consequences for this medical specialty still fully in development. Bombing in 1940 destroyed several buildings of the Wilhelmina Gasthuis in Amsterdam. The surgical institute was confiscated by the German *Luftwaffe* and used as a military hospital. The increase of infectious diseases put extra pressure on the remaining beds. Sometimes hospital beds were used as a cover for people in hiding, pretending they had undergone brain surgery by bandaging their head. Hospital personnel risked capture by the Germans (the surgeon, W. Noordenbos Sr.) or had to escape, as Oljenick did. What remained of the hospital suffered badly from poor functioning. In 1941, the name of the Wilhelmina Gasthuis had to be changed to Westergasthuis, because the use of the Queen's name was forbidden. In Utrecht and Rotterdam, too, considerable parts of the hospital were destroyed at the beginning of the war. In Utrecht, the neurological-psychiatric institute, including neurosurgery, was scattered over various other hospitals throughout the town for the duration of the war and some time thereafter. The surgical department in Rotterdam had to be accommodated in several Rhine barges moored in the *Coolhaven*. The neurological department was housed in a former Jewish old people's home. The neurosurgeon M. Weersma had to set up a neurosurgical department in the same building years later, in 1951. The St. Ursulakliniek in Wassenaar was considerably affected by bombings of government buildings and embassies in the vicinity and by the billeting of the Germans throughout the war.

At the beginning of the war, two neurosurgical residents were in training with Lenshoek in Amsterdam: P.M. Hoeberechts and H. Verbiest. Two others were appointed during the war: P.R.M.J. Hanraets in Wassenaar and W. Noordenbos Jr. in Amsterdam.

Paul M. Hoeberechts was appointed by Oljenick in 1938 having studied general surgery for a few years. After Oljenick's escape, he stayed briefly with Lenshoek in Amsterdam, moving to Wassenaar in 1941 as a temporary replacement for De Vet who was taken ill for a long period. After completion of his training in 1942 he became De Vet's associate. This collaboration subsequently failed because Hoeberechts felt he was regarded as subordinate and that his ability was underestimated, only being allowed to perform lower back surgery. With the support of the neurologist, J. Prick, he started a neurosurgical practice in the Canisius Hospital in Nijmegen on 5th September 1942. Here he had a separate 22-bed unit, some children's beds, and private beds at his disposal. Quite an active man, he had already performed 301 neurosurgical procedures by 1945. According to Hanraets, one of the few who knew him quite well, Hoeberechts was a skilled and fast-working surgeon, but his capacities often went unappreciated, probably because of his tacit nature. He had no interest in surgery of gliomas and disliked doing low back surgery. He had to leave Nijmegen in 1951 because of an extramarital relationship. He moved to Toronto, Canada allegedly because of the fear of a Russian invasion – where he continued to practise neurosurgery. At the urgent request of J.J.G. Prick, neurosurgery in Nijmegen was kept afloat by M.P.A.M. de Grood and by De Vet and Hanraets from Wassenaar. In 1956, neurosurgical practice at the University Hospital and at the Canisius Hospital was taken over permanently by H.A.D. Walder, trained in Wassenaar.

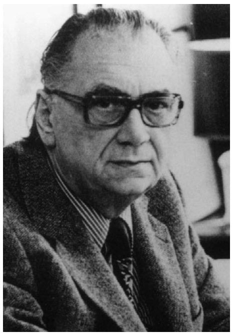


Figure 14. Prof. Dr. H. Verbiest, neurosurgeon in Utrecht from 1942 till 1981.

Henk Verbiest (1909-1997, Fig. 14) was born in Rotterdam and studied medicine in Leiden. He also followed lectures in philosophy for a number of years, which left their mark on him for life. He trained in neurology under the lecturer A. Gans and under Prof. G.G.J. Rademaker in Leiden. His doctoral thesis (1939) was neurological: *The influence of the posterior funiculus system on the tonic cortico-spinal innervation of the limbs. The flexion phenomenon of the fingers*. This thesis gave rise to the eponym 'Verbiest sign' (pseudo-athetosis of the fingers due to lesion of the cervical posterior funiculus system). Probably because of his broad knowledge of the nervous system, Rademaker urged him to train in neurosurgery with Clovis Vincent. But, as a result of the war, this training was scattered over a number of cities: Paris, Utrecht, Amsterdam and again Utrecht for a surgical year in the Deaconess Hospital. In 1942, the neurologists Sillevis Smitt and Van der Does de Willebois allowed him to settle as a neurosurgeon in the neurological institute of the University Hospital in Utrecht. It was here that he would build an impressive career over a period of 39 years. He became internationally known for the Verbiest Syndrome' (neurogenic intermittent claudication due to developmental stenosis of the lumbar vertebral canal), his anterior and antero-lateral approach to the cervical spine and the resection of affected cervical spinal bodies, and the transoral approach to the dens. He delivered hundreds of lectures all over the world and published numerous papers in many international journals and books. In 1949 he was appointed lector of neurosurgery and read a remarkable paper, entitled: *The development of neuro-surgical behaviour*, revealing his philosophical background. He became full professor of neurosurgery in 1963 with an inaugural speech: *Claude Bernard and functional neurosurgery*. He had many doctoral students and trained a large number of neurosurgeons. In the Dutch-speaking region, these included: W. Luyendijk (Leiden, later professor of neurosurgery), L.J.E. Calliauw (Bruges, later professor of neurosurgery in Gent, Belgium), L.N.M. Coene (Heerlen), R.C. Kruyt (Rotterdam, Enschede), N.J. Bosma (partially, Utrecht), H. Ponssen (Amsterdam, Utrecht), Th.A. Dokkum (Utrecht), C.W.M. van Veelen (Utrecht, later professor of neurosurgery), W. Pondaag (Zwolle), J.W. van 't Verlaat (Utrecht, Malta), H.D. Mayer (Tilburg) and P.H.J.M. Elsenburg (Utrecht). Verbiest retired from university in 1981, at the unusually old age of 72, with a valedictory speech: *Between mirror and window*. But he continued lecturing, publishing and working as an adviser and as the chief editor of his own international journal *Neuro-Orthopedics*, almost until his death in 1997. C.A.F. Tulleken succeeded him as professor and head of department in Utrecht. Verbiest was a strong and dominant personality, who called himself a benevolent despot. He received numerous decorations, awards and honorary memberships at home and abroad, including the honorary membership of the *Nederlandse Vereniging van Neurochirurgen,* the honorary presidency of the World Federation of Neurosurgical Societies, and the Catharijne Prize from the University Hospital Utrecht for his great merits in the field of neurosurgery, presented to him by H.R.H. Prins Bernard of the Netherlands, a prize which gave him the greatest satisfaction.

Paul R.M.J. Hanraets (1914-1995) was born in Weert and studied medicine at the Municipal University of Amsterdam, where he met De Vet, who trained in Amsterdam at that time. He started his neurosurgical training with De Vet in the St. Ursulakliniek in Wassenaar in May 1941. After four years in neurosurgery, he spent two years in general surgery in various locations in Spain, Italy and Paris. He settled in Wassenaar in May 1947, initially as De Vet's associate. After a few years, he severed this association for financial reasons and continued to practice neurosurgery in Wassenaar on his own. He spent a year in Batavia, Dutch East Indies in 1949 to practise neurosurgery, fulfilling a governmental agreement between The Hague and Batavia. Hanraets was a skilful neurosurgeon. He was known in the Dutch medical body for his radical low back surgery with wide laminectomies and foraminal decompressions. His doctoral thesis (1959) was a comprehensive monograph bearing the title: *The weak back. A medical study of the endogenous components of disorders of the back, which is then called: a degenerative back*. He was also known among colleagues for his cerebellopontine angle surgery, especially the Dandy operation for trigeminal neuralgia. Contrariwise, he did not believe in the surgical treatment of cerebral gliomas, because of the high mortality rate immediately postoperative (which was higher than 30 per cent in those days), and the very poor long-term results. He found that surgical mortality was much lower if a wide dural decompression was carried out. With the exception of his thesis, Hanraets published almost nothing. During his career in Wassenaar, he and De Vet were both responsible for the training programme. Hanraets was very active and often quite violent in matters of financial and professional interest. He had a short-temper and his emotions often ran high. At the end of his career he felt rather disappointed in neurosurgery, which was the reason for his untimely retirement in 1975. He spent the rest of his life on the island of Corsica. His successors in Wassenaar were M.Th.A. van Duinen and C.A.F. Tulleken.

Figure 15.
Prof. Dr. W. Noordenbos, neurosurgeon in Amsterdam from 1946 till 1976.

William Noordenbos (1910-1989, Fig. 15) was born in Utrecht, son of a future professor of surgery at the University of Amsterdam, W. Noordenbos Sr. He began his medical study in Amsterdam, but after a few years his father judged it better for him to continue in Anglosaxon surroundings. Therefore, William went to Edinburgh in 1937, a move that left its mark for the rest of his life. In 1940 he had to return to Amsterdam where he finished medical school one year later. He returned to Scotland for his surgical training and completed it under his father's supervision in the Wilhelmina Gasthuis. When his father died in 1944, he turned to neurosurgery with Lenshoek. W. Noordenbos Sr. had not had a very high opinion of this branch of surgery, and when talking about removing a brain tumour he used to say: "it is like taking a starfish out of a cup of butter" (De Grood 1977). After finishing his training in 1946, Noordenbos became Lenshoek's associate. They were quite different personalities, a contrast expressed in many rows in later years. Both of them worked not only in the University Hospital with the neurologists B. Brouwer and A. Biemond, but also in the Nursing Home Prinsengracht and the Valerius Clinic (neurologist-psychiatrist L. van der Horst) in Amsterdam, in the Coolsingel Hospital in Rotterdam (neurologist B.G. Ziedses des Plantes) and occasionally in Wassenaar. During Lenshoek's stay in Dutch East India 1947-1948, Noordenbos was acting head of the department. He later relieved Lenshoek in Batavia for six months. When Lenshoek left for Groningen in January 1955, Noordenbos became head of the department. He obtained his doctor's degree with a thesis: *Pain. Problems pertaining to the transmission of nerve impulses that give rise to pain* (1959). He called this book a preliminary statement. The subject would capture his interest for life. One of his closest friends was Patrick Wall from London, who with Ron Melzack from Montreal formulated the gate-control theory of pain in 1965. Noordenbos was appointed Lecturer in Neurosurgery in 1960, with the inaugural lecture: *Some aspects of the surgery of the central nervous system*, and on becoming Ordinarius of Neurosurgery in 1965, his inaugural speech was called *Neurosurgical development*. He was an excellent clinical diagnostician, a deliberate and cautious surgeon, and an ardent sea yachtsman. He did not have the ambition to compete with the giants in the area of neurosurgical techniques. His most important publications were on the problem of pain (1959). He was a rather uncommunicative person, who appeared to be somewhat stiff to those who did not know him well. During his years with Lenshoek, Noordenbos was involved in the training programme of De Grood (1947-1951), and Van Hoytema and De Lange (1949-1953). From 1955 onwards, he himself trained a great number of neurosurgeons: T.A. Lie (Tilburg), A.J.M. van der Werf (Amsterdam, his future successor), P.J. Vinken (the future president of the board of directors of the Elsevier Publishing Company), R. Braakman (Rotterdam, later professor), J. Oostrom (Enschede), A.C.J. Slooff (Heerlen), L.M. Vencken (Tilburg, who later turned to neuroradiology), H.A.M. van Alphen (Amsterdam, future professor at the Vrije Universiteit), R. Dreissen (Amsterdam), R.E.H. van Acker (Amsterdam), and J.F. Ploegmakers (Amsterdam). From its formation in 1952, Noordenbos was the secretary of the *Nederlandse Vereniging van Neurochirurgen* for 15 years. He also was one of the founders of the International Association for the Study of Pain and was later appointed honorary member. Noordenbos abdicated as professor and head of department in 1976, but he continued working on his beloved subject of pain. A.J.M. van der Werf, who was already appointed Lector of Neurosurgery in 1970, succeeded him as head of the department and became full professor in 1982.

The period 1945–1952

The post-war period was not only a time of clearing up and reconstruction, but also of reconsidering the position of neurosurgery within the scope of a boom in medicine. The number of brain tumours detected, which was the foundation of neurosurgery in Cushing's time, was still increasing due to improved and earlier diagnosis, but played a relatively minor part in neurosurgical practice. There was a clear swing to psychiatric surgery, sympathetic surgery and spinal surgery. The increasing number of neurosurgical patients required more beds and personnel in the neurological-neurosurgical centres, at the expense of neurology. Especially patients for lumbar disc and peripheral nerve surgery could no longer be accommodated in these centres, and they had to be operated on in other hospitals. Neurologists referred more and more patients directly to the neurosurgeons. For these reasons the neurosurgeons wanted to arrange their own out-patient clinics and the larger workload meant an increasing requirement for neurosurgical manpower. All these developments exerted considerable pressure on the working relationship between neurologists and neurosurgeons in the different centres.

Dutch neurosurgeons also had commitments in Dutch India, which was still part of the Netherlands after the war. Lenshoek, who was born in Dutch India and who maintained strong ties with the neurologist Prof. P.M. van Wulfften Palthe in Batavia, went to his native country in 1947 to survey the situation and to meet the most urgent neurosurgical needs. However, Lenshoek also showed sympathy for the Indonesian independence movement. This made him *persona non grata* for the military command. The Dutch Indian authorities threatened to summon a neurosurgeon under permanent appointment from the mother country. Back in Holland, Lenshoek discussed this matter with other neurosurgeons, and Van Wulfften Palthe came to Holland for consultation with Prof. Brouwer in August 1948. A written agreement, adopted unanimously by all neurosurgeons, stated that they would serve in Dutch India on a rotational basis for 6 to 12 months. Accordingly, after Lenshoek, Noordenbos, Hanraets, De Vet, Weersma and De Grood went to Dutch India. All contracting parties also agreed that De Vet in Wassenaar should train the Indonesian surgeon Handojo as a neurosurgeon, so that, in the future, Handojo together with one of his Dutch colleagues could cover neurosurgery in the Dutch Indies. During the discussions in 1948, De Grood indicated that he would be prepared to settle in the Dutch colony permanently after finishing his training in Amsterdam, if his time there would prove satisfying. It did not, however, come to this, because everything had changed in the Dutch East Indies by that time. The second police action between December 1948 and February 1949 had caused a dead-end situation there for the Dutch. On 27th December 1949 sovereignty was transferred and Indonesia became independent. Lenshoek went back to Indonesia in the early part of 1951, and provisionally assumed control of the neurosurgical department in Djakarta. However, Van Wulfften Palthe, who had retired as neurologist, advised the Dutch neurosurgeons to ask the Indonesian government officially whether they wished the Dutch neurosurgical support to continue. This led to a long discussion in the *Study Club*. The neurologists Hoelen and Sillevis Smitt were of the opinion that the agreement was no longer valid. They no longer wanted to lend their neurosurgeons in this way. The letter to the Indonesian government, as proposed by Van Wulfften Palthe, was indeed sent, but no official agreement was reached. Handojo finished his training in Holland and started to practise in Djakarta mid-1952. The direct involvement of Dutch neurosurgeons in Indonesia ended at this time.

In the meantime, several new residents were taken into neurosurgical training in different centres in Holland. In Groningen, *A. van der Zwan* had been trained as a neurologist before the war. In 1940 he obtained his doctoral degree with a thesis, entitled: *On the genesis of anencephalia and rachischisis posterior and anterior.* There was a gentlemen's agreement that he should practise as a neurologist in the University Hospital in Groningen during the war and would then be trained in neurosurgery after the war. Supported by a grant from the Rockefeller Foundation, the medical faculty sent him to Hugh Cairns and Joe Pennybacker in Oxford, England where he trained from January 1946 until the end of 1948. On his return to Groningen he was appointed Lector of Neurosurgery. However, the hospital facilities were very poor and the neurologist Droogleever Fortuyn backed by the psychiatrist Kraus did not allow him to make rounds or to look after his own patients. Nor was he allowed to teach the students. Ample reasons for Van der Zwan to leave Groningen in 1954 and establish a new neurosurgical department in Zwolle, where he practised neurosurgery until his retirement. Lenshoek succeeded him in Groningen in 1955.

In 1946 *M. Weersma*, who was a neurologist-psychiatrist practising in Leeuwarden, was engaged by De Vet in Wassenaar. After finishing his training in 1950, he fulfilled his turn as neurosurgeon in Indonesia. In 1951 he settled in Rotterdam, where the neurologist Ziedses des Plantes wanted to have his own neurosurgical unit in the Coolsingel Hospital. But Weersma had to start his neurosurgical career in the temporary housing of the neurological department, called De Schietbaanlaan, named after the street in which it was located. After about two years the neurologists were not happy with his work and results, partly due to Weersma's psychiatric background, and refused to refer any more patients to him. He was dismissed in 1953, but continued practising on his own in the Municipal Hospital in Schiedam until his retirement.

M.P.A.M. de Grood started his neurosurgical training in Amsterdam in 1947, having been trained as a general surgeon in Tilburg during the war. After some short locum tenencies in Djakarta and Nijmegen, he finally settled in the St. Elisabeth Hospital in Tilburg in 1952. He built up an enormous practice and performed neurosurgical procedures in many hospitals throughout the southern part of the Netherlands. De Grood's doctoral thesis in 1966 was entitled: *The indication for operative treatment of saccular aneurysms of or near the circle of Willis*.

G.J. van Hoytema and S.A. de Lange started their training in Amsterdam in 1959 after training in general surgery. *Van Hoytema* practised as a general surgeon in Soerabaja, Dutch India for four years after the war, before embarking on neurosurgical training. In 1953 he settled in Enschede where he founded a new neurosurgical centre. His doctoral thesis in 1956 was on *Hydrocephalus*. In 1953 *De Lange* filled the Rotterdam vacancy caused by Weersma's departure. A newly built municipal hospital with an independent neurosurgical department was opened there in 1961. This hospital became the university hospital in 1967. De Lange defended his doctoral thesis: *Operative treatment of progressive hydrocephalus with ventriculo-cardial drainage using the Spitz-Holter valve system* in 1965 and was appointed Professor of Neurosurgery in 1968.

The neurologists observed these developments with suspicion and were concerned about this neurosurgical expansion. Sillevis Smitt, for instance, was afraid that the number of neurosurgeons was increasing too rapidly and that they were receiving too much training in neurology, with the risk that they would be forced to practise neurology in the future. Brouwer, on the other hand, was of the opinion that even more neurosurgeons would be needed for Dutch India as well as for South Africa in near future. This interference of the neurologists in neurosurgical professional interests caused more and more friction in the first post-war years resulting in a letter sent by the joint neurosurgeons to Brouwer as the president of the *Study Club* in October 1948. They pointed out, that the neurologists' interference was slowing down the development of neurosurgery in technical and organisational respects. Due to spatial limitations, neurosurgery was scattered over too many hospitals, and due to the shortage of manpower, the neurosurgeons could not participate in scientific research. As a consequence, neurosurgery in the Netherlands was threatening to slide back into the pre-Cushing era. They argued in favour of a drastic reorganisation of the existing neurosurgical departments with management fully and exclusively entrusted to the neurosurgeons. The set-up and personnel would have to be improved, depending on the local circumstances. Close cooperation with the neurologists, on the other hand, was judged to be both desirable and necessary. In reply to this letter, the neurologists Biemond and Prick wrote a memorandum. Prick stated quite frankly that neurosurgical education at that time was totally inadequate to guarantee proper neurological diagnostics or correct indications for neurosurgical treatment. On the contrary, it entailed many risks. Biemond's reply was more diplomatic. Protracted discussions followed in the meetings of the *Study Club*, but without actual results, except for the fact that De Vet was appointed as the first neurosurgical member of the Specialists' Registration Committee in October 1948. In September 1949, Prick wrote the article in the *R.K. Artsenblad*, which was referred to at the onset of this chapter. Hoeberechts' reaction was venomous. Brouwer, who had appeared to be the binding force in this conflict of interests, died suddenly on 1st November 1949, after which the differences between neurologists and neurosurgeons escalated. This finally resulted in a second letter from the joint neurosurgeons to the secretary of the Dutch Study Club for Neurosurgery, saying: "All considerations have led to the opinion that it is necessary to found a Dutch society of neurosurgeons separate from the existing Study Club. The objectives of this society can be formulated as follows: a. the protection of the social and professional interests of the Dutch neurosurgeons as well as of the specialty of neurosurgery, in the same way as for other specialties; b. the organisation of scientific meetings open to every medical doctor interested in neurosurgery; c. the establishment of relations with Dutch societies of medical specialties and with foreign neurosurgical or other medical societies." The Dutch Society of Neurosurgeons was founded during a first business meeting on Friday 28th November 1952. The next day, the foundation was discussed at the 39th meeting of the The Netherlands Study Club for Neurosurgery. The neurologists could only express their disappointment and regret about the state of affairs. The emancipation of neurosurgery in the Netherlands was an accomplished fact (Fig. 16).

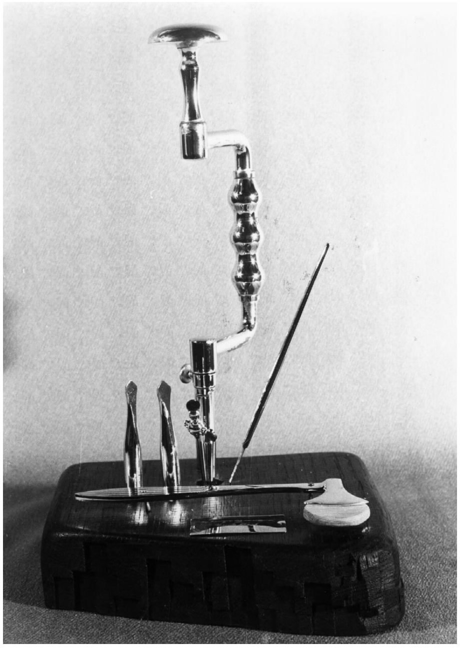


Figure 16.
Present from Prof. Dr. A. Biemond, president of the Netherlands Society of Neurology, to the newly-founded Netherlands Society of Neurosurgeons in 1952.

Epilogue

Since the formation of the Netherlands Society of Neurosurgeons, neurosurgery in the Netherlands has seen an incredible evolution. The number of fully trained neurosurgeons has increased from eleven in 1953 (Oljenick and Hoeberechts had left the country) to 93 in 2002, some 20 being in training, for a population of 16 million. The number of neurosurgical centres and smaller neurosurgical departments rose from nine to 16 in the same period (Table 1). In addition, many minor neurosurgical procedures, including spinal surgery, are carried out in other community hospitals. At least all major centres are equipped with modern devices, including facilities for radiosurgery with either the gamma knife or linear accelerator in three hospitals. Gradually, a subspecialisation occurred in different branches of neurosurgery. Nowadays the Netherlands Society of Neurosurgeons has official sections for paediatric neuro-

Table I. State of Neurosurgery in the Netherlands as of April 2002.

Site	Number of Neurosurgeons
Academic Neurosurgical Centres	
Academisch Medisch Centrum, Amsterdam (chairman: Prof. Dr. D.A. Bosch)	6
Vrije Universiteit Medisch Centrum, Amsterdam (chairman: Prof. Dr. W.P. Vandertop)	7
Academisch Ziekenhuis Groningen, Groningen (chairman: Prof. Dr. J.J.A. Mooij)	6
Leids Universitair Medisch Centrum, Leiden (chairman: Prof. Dr. R.T.W.M. Thomeer)	6
Academisch Neurochirurgisch Centrum Limburg, Maastricht (chairman: Prof. E.A.M. Beuls)	9
Neurochirurgisch Centrum Nijmegen, Nijmegen (chairman: Prof. Dr. J.A. Grotenhuis)	7
Academisch Ziekenhuis Rotterdam, Rotterdam (chairman: Prof. Dr. C.J.J. Avezaat)	11
Universitair Medisch Centrum Utrecht, Utrecht (chairman: Prof. Dr. C.A.F. Tulleken)	9
Neurosurgical Centres and Departments in Regional and Community Hospitals	
Medisch Centrum Alkmaar, Alkmaar	3
Slotervaart Ziekenhuis, Amsterdam	3
Medisch Centrum Haaglanden, Den Haag	5
Leyenburg Ziekenhuis, Den Haag	2
Medisch Spectrum Twente, Enschede	4
Martini Ziekenhuis, Groningen	3

surgery, spinal neurosurgery, pain and tumours of the nervous system. The association has some ten professional committees and many representations in national and international organisations. The Netherlands Society of Neurosurgeons has been a member of the World Federation of Neurosurgical Societies and of the European Association of Neurosurgical Societies from their foundation in 1955 and 1971, respectively. Several Dutch neurosurgeons have played an active role in both organisations from the beginning. Luyendijk was elected president of the WFNS in 1981, after having served as its secretary for eight years. Walder served as the treasurer of the EANS for eight years and as the secretary of the WFNS for 12 years, and Van Alphen secured the organisation of the 11th World Congress of Neurosurgery for our country in 1991, and which was held under his presidency in Amsterdam in July 1997. All three were elected honorary presidents and successively served as historians of the World Federation. In addition, Van Alphen held the offices of treasurer, vice-president and president of the Academia Eurasiana Neurochirurgica for 13 years and organised its Ninth Convention in Houthem-St Gerlach, near Maastricht in July 1998.

The *Netherlands Society of Neurosurgeons* will celebrate its 50th anniversary on 28th November 2002. This part of the history of neurosurgery should be described in detail in another context later.

Much of the information for this chapter was obtained by the author from the archives of the Netherlands Study Club for Neurosurgery and through written and oral personal communication with the individuals in question.

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	METHODS	HISTOLOGY OF NERVOUS TISSUE	MICROSCOPAL TOPOGRAPHY AND COMPARATIVE ANATOMY
		1718 van Leeuwenhoek, nerve fibers	
1800	1809 Reil, ethanol fixation		
	1830 Lister, achromatic objective	1833 Ehrenberg, identifies nerve cell bodies	
		1837 Remak, identifies axons	
		1838 Purkinje, names axons 1838 Purkinje, Valentin, dendrites emanate from somata	
	1840 Hannover, chromic acid/salts fixation	1838 Remak, nerve fibers emanate from somata 1842 Helmholtz, nerve fibers emanate from somata	
	1843 Stilling, serial sectioning	1843 Hannover, nerve fibers emanate from somata	1843 Stilling, Ueber die Medulla oblongata
1850	1851 Waller, secondary degeneration	1865 Deiters, distinguishes the essential differences between axon and dendrites as protrusions of the nerve cell body	
	1858 Gerlach, carmine staining 1869 Klebs, paraffin embedding		1851 Türck, Ueber secundäre Erkrankung einzelne Rückenmark Stränge
	1870 Duval, collodion (celloidin) embedding von Gudden, method of secondary atrophy		1867/8 Meynert, Der Bau der Grosshirnrunde 1876 Flechsig, Die Leitungsbahnen im Gehirn und Ruckenmark auf Grund entwicklungsgeschichtlicher Untersuchungen
	1873 Golgi impregnation 1882 Weigert, myelin stain		1885-1900 Edinger, Vorlesungen über der Bau der nervösen Centralorgane des Menschen und der Thiere
	1885 Nissl, methylene blue stain Marchi and Algeri, stain for degenerating myelin	1887 Forel, neuron theory 1889 His, neuron theory	1890/1 Dejerine, Anatomie des centres nerveux 1891 Judson Herrick, Journal of Comparative Anatomy
	1886 Ehrlich, intravital methylene blue method His, microtome	1888-1909/11 Cajal, substantiates neuron theory dynamic polarization of nerve cells	1893 van Gehuchten, Anatomie du système nerveux 1894 von Bechterew, Die Leitungsbahnen im Gehirn und Rückenmark
	1891 Cox, modification of the Golgi method	1891 Waldeyer, coins the term "neuron"	1896 von Koelliker, Vom Nervensysteme
	1893 Blum formalin fixation		1896 Obersteiner, Anleitung beim Studium des Baues Nervösen Centralorgane 1897 von Monakow, Gehirnpathologie
1900	1902 Bielschowski, reduced silver method	1900 Sherrington, the "synaps," conducts in one direction only	1909/11 Cajal, Histologie du système nerveux
	1904 Horsley and Clarke, stereotaxic instrument	1906 Langley, nicotine and curare "receptors"	1917-1928 Winkler, Neurologie
	1919 Del Rio Hortega, ammonical silver method	1919 Del Rio Hortega, microglia, oligodendroglia	
	1941 Gomorri, introduction enzyme histochemical methods	1935 Dale, each neuron releases only one type of synaptic transmitter	1936 Ariëns Kappers, Huber and Crosby, The comparative anatomy of the nervous system of vertebrates including man
1950	1950 glutaraldehyde fixation, plastic embedding and osmium staining for electron microscopy	1950 Palade, Palay, ultrastructure of the synaps	
	1954 Nauta and Gygax, selective silver impregnation of degenerating axons	1953 Eccles, inhibitory and excitatory neurons IPSP and EPSP 1963 Bennett et al., gap junctions	
	1962 Falck and Hillarp fluorecense of monoamines		
	1968 Lasek, autoradiography of antegradely transported tritiated aminoacids		
	1971 Kristensson and Olson, retrograde axonal transport of horseradish peroxidase		
	1970 Sternberger et al., immunohistochemical technique		1976 Peters, Palay and Webster, The fine structure of the nervous system
	1984 Kuypers, introduction of fluorescent tracers for double retrograde labeling of neurons		
	1990 Kuypers and Ugolini, viruses as transneuronal tracers		1998 Nieuwenhuys, , ten Donkelaar and Nicholson, The central nervous system of vertebrates
	1992 Valentino et al., in-situ hybridization technique2000		
2000			

Table I. Tabulated summary of the history of neuroanatomical methods and techniques, the 'ideogenesis' of the neuron and the development of topographical and comparative neuroanatomy. 1) First part of this column is copied from van der Loos 1967

Neuroanatomy

8

J. Voogd

The history of neuroanatomy in the Netherlands, like that of other scientific disciplines, is the history of people and their ideas. Only a few gifted scientists occupy the centre of the stage; their scientific progeniture occupies many of today's chairs of Neurology and Anatomy. Their ideas and interests, which inspired their contemporaries, have often lost some of their glamour. In some cases, however, there has been a continuity of the topics of the research throughout the generations. This continuity, and the emergence of completely new initiatives, is the subject of this review. Dutch neuroanatomy is not an isolated affair; it participates in the international development of concepts and techniques. Achievements of Dutch neuroanatomists, therefore, should be viewed against the background of events elsewhere in the world. The first section of this review is a rough sketch of these international developments from the early 1800s onwards. It begins with the introduction of the compound microscope and the use of achromatic objectives by Lister, in 1830. Indeed, neuroanatomy is a science of microscopy, just as astronomy is non-existent without the telescope. The description of the gross anatomy of the central nervous system, which was almost complete around that time, accordingly, will not be considered in this chapter. Dutch contributions to this field were reviewed in the monograph of Schulte and Endtz (1977). Publications on neuroanatomy and related subjects from the period of approximately 1850 up to 1937 are listed in the bibliographies of Mesdag (1923) and Bouman (1937). The main international developments in neuroanatomy are summarised in Table I. Table II depicts the genealogy of Dutch neuroanatomists.

International developments

The emergence of new methods to study the microscopical anatomy and the histology of the brain, the development of ideas about the histology of nervous tissue, and the growing interest in the microscopical topography of the central nervous system have been summarised in the three, more or less synchronous time-columns of Table I. More complete reviews and the references to these topics can be found in the monographs of Clarke and O'Malley (1968), Haymaker and Schiller (1970), Bracegirdle (1978), Shepherd (1991) and Jacobson (1993). The early history of the histology of the nerve cell is copied from Van der Loos (1967).

With a few exceptions, there are no Dutch among the scientists who developed the field in the 19th century. It is almost exclusively an affair of the German-speaking world. Most of the techniques for ethanol and chromic acid fixation, which remained in

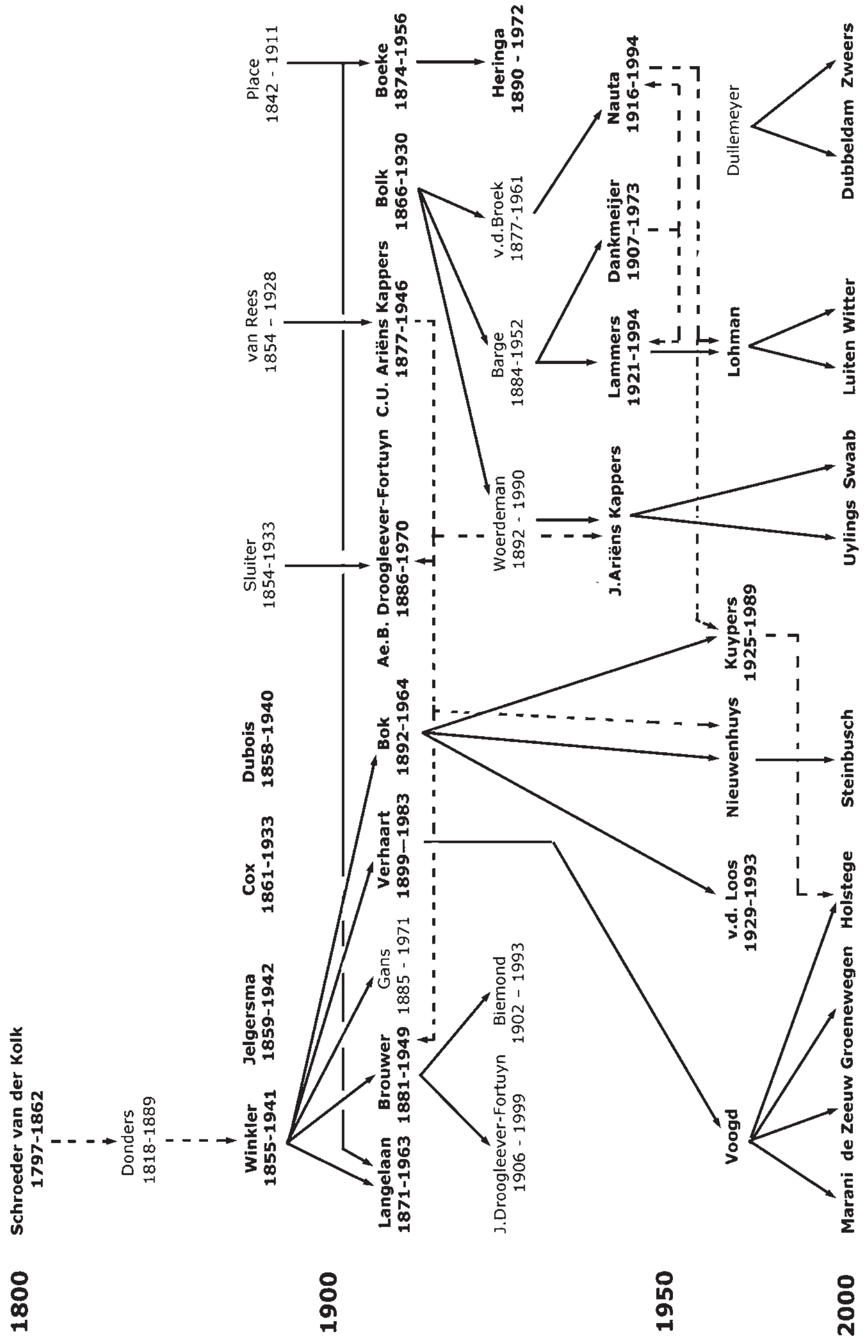

Table II. The genealogy of Dutch neuroanatomy.
Only scientists who occupied academic chairs or lectureships are included, with the exception of Cox. Those who found one of their main occupations in neuroanatomy are in bold print.

common use till Blum introduced formalin as a fixative in 1893, serial sectioning, the staining of nervous tissue with carmine and with Ehrlich methylene blue, as in the Nissl method, the introduction of the aniline–dye 'Perkin's mauve" by Beneke (1862), Weigert's myelin stain, embedding in paraffin and celloidin (introduced by Duval in 1870, and improved by Schiefferdecker in 1882), were discovered in German laboratories. These improvements in histological techniques favoured studies on the microscopical topography and the comparative anatomy of the brain and the spinal cord, starting with the beautiful volumes of Stilling (1842b, 1843, 1846, 1864-1878) illustrating unstained, serial sections of the cord, the medulla oblongata, the pons and the cerebellum in unsurpassed detail, followed by the textbooks of Meynert (1867/8, "Erst seit Meynert ist das Gehirn beseelt" [Meynert blew the breathe of mind into the brain]) , his pupil Flechsig (1876) and his second-generation student von Bechterew (1898). Meynert, Flechsig and von Bechterew, like other authors of texts on the topography of the central nervous system such as Obersteiner, von Monakow and Dejerine, were clinicians, who fostered the hope that the advances in neuroanatomy would explain nervous and mental diseases. The comparative anatomical studies of the nervous system of Judson Herrick who, together with his brother Clarence, founded the *Journal of Comparative Neurology* in 1891, and Edinger were also facilitated by these techniques.

Türck's (1850, 1851a,b) observation of granule cells in degenerating pyramidal tract and some ascending spinal fiber systems of the cord, and Waller's discovery in the same year of his method of secondary degeneration (a "New method for studying the nervous system which can be applied to research of the distribution of the nerve columns"), paved the way for the tracing of nervous connections. Von Gudden's (1870) method of secondary atrophy of tracts and nuclei, upon removal of parts of the brain in young animals, introduced the experimental approach in neuroanatomy. Most influential, however, was the myelogenetic method, introduced by Flechsig and extensively used by von Bechterew and Edinger, which allowed the tracing of pathways in the central nervous system of human feotuses, neonates and young children, who acquire their myelin sheaths at different dates. The discovery by Marchi and Algieri (1885) that degenerating myelin, mordanted with potassium dichromate, could be stained with osmium, was the birth of modern tract tracing. Retrograde changes in nerve cells were observed with the Nissl method, published in the same year. As Gowers (1845-1915) remarked "We may learn as much of the course of fibres by studying them in their birth as in their death – in their development as in their decay" (cited by Haymaker and Schiller 1970).

The anterograde and retrograde tracing of fibre connections, implies knowledge of the origin of nerve fibres from nerve cells. This notion took a long time to become established knowledge. Van der Loos's (1967) account of the ideogenesis of the nerve cell has been used for the early part of the time-column in Table 1; references on this period can be found in his paper. Starting from van Leeuwenhoek (1718), ideas about nerve fibres and nerve cell bodies follow a separate course. Observations on the origin of the nerve fibre from the cell body culminated in Deiters' (1863) description of the essential differences in the morphology of the axon and the dendrites as prolongations of the nerve cell. Van der Loos (1967) noticed that Deiters found a second system of small axons that took their origin from the dendrites. These small axons probably represent terminals on the dendrites, but, at the time, they were considered rather as part of a reticulum, connecting all neurons. The neuron theory, "the enlightened idea that the expansions of nerve cells end freely in the grey substance just as they do in the peripheral sense organs" (Cajal 1954), was formulated by Forel (1887) and His (1889) and epitomised by Waldeyer (1891). Forel based his concept on experimental studies with the von Gudden method of secondary atrophy; the ideas of His were derived from embryological studies. Cajal, in monumental studies, substantiated and extended the neuron theory for most systems in the brain.

Remarkably, the advances in histological techniques scarcely contributed to the development of ideas on the morphology of the nerve cell in the early 19th century. Most of its students used free hand dissection to isolate nerve fibres and nerve cells. The change was made by Golgi's discovery in 1873 of the 'reazzione nera', the intravital methylene blue stain by Ehrlich (1886), and their adoption by Cajal.

The 1850-1900 surge in the development of neuroanatomy ended with the discovery and the application of the reduced silver methods by Bielschowsky (1902), Cajal (1903), del Rio Hortega (1919) and with the publication of *Histologie du système nerveux* by Cajal (1909/11).

The long period of relative neuroanatomical silence, which lasted throughout the interbellum and the the Second World War, saw spectacular developments in the electrophysiological techniques and the ideas about nervous transmission. It followed Sherrington's discovery (1900, 1906) that the synapse conducts in one direction only, refuting Cajal's hypothesis that the direction of conduction (the dynamic polarisation) is a property of the neuron. In the Netherlands, however, neuroanatomy flourished in this period, and saw the production of Winkler's *Textbook of Neurology* (1917-1928) as well as the codification of comparative neuroanatomy by Ariëns Kappers, Huber and Crosby (1936).

The second half of the 20th century observed a 'second flowering' (Nauta 1993) of neuroanatomical research, where the focus moved from Europe to the United States. With improved methods for tissue preparation, electron microscopy of nervous tissue became possible, which confirmed the neuron theory and clarified the structure of the synapse (Palade and Palay 1954). Tract-tracing methods made it possible to analyse connections with increasing detail. In this field, Nauta, Kuypers and other Dutch scientists made notable contributions. The demonstration by Eccles (1953) of separate classes of inhibitory and excitatory neurons, in combination with enzyme histochemistry, fluorescent microscopy, immunocytochemistry and in-situ hybridisation, made it possible to approach nervous transmission with combinations of electrophysiological and morphological techniques. Dutch descriptive and comparative neuroanatomy flourished in these years, culminating in the recent monumental publication by Nieuwenhuys, ten Donkelaar and Nicholson of the *Central Nervous System of Vertebrates* in 1998.

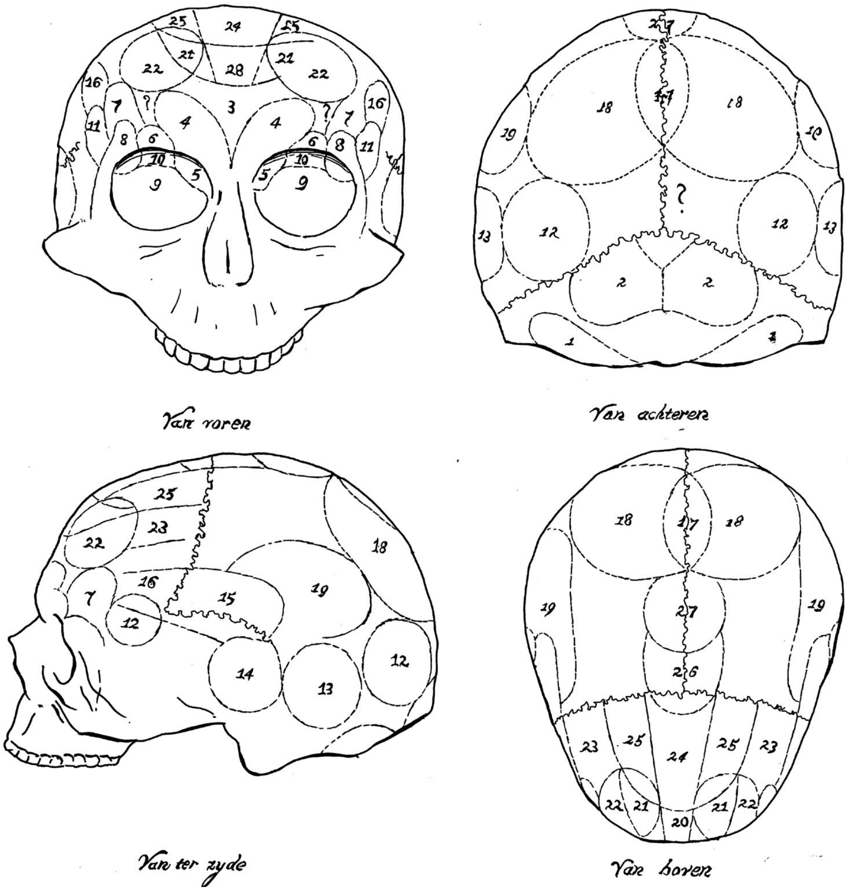

Figure 1.
Localisation on the skull of the different mental organs distinguished in the lectures by Gall. From Stuart (1806), retouched. The location of the sense of art (11) and music (7), the sense of murder (14), and the sexual drive (1) are indicated. Higher mental functions, such as comparative intelligence (20) and benevolence (24) are located frontally and dorsally.

The early years: Schroeder van der Kolk

Between the 8th and the 18th of April 1806, Frans Joseph Gall lectured in Amsterdam on the brain as a collection of the various organs of the mind, in the auction room of an inn, 'the Amsterdam Arms'. In his anatomy of the brain, special faculties of the mind are localised at special sites. The surface of the skull makes it possible to decide about the state of these different organs. Most of them are present in the brains of both animals and humans. The senses of art and music, located in the lower frontal region, are strongly developed in beavers and singing birds respectively (Fig. 1). Sexual drive is located in the cerebellum; the broad neck of Turkish men is related to

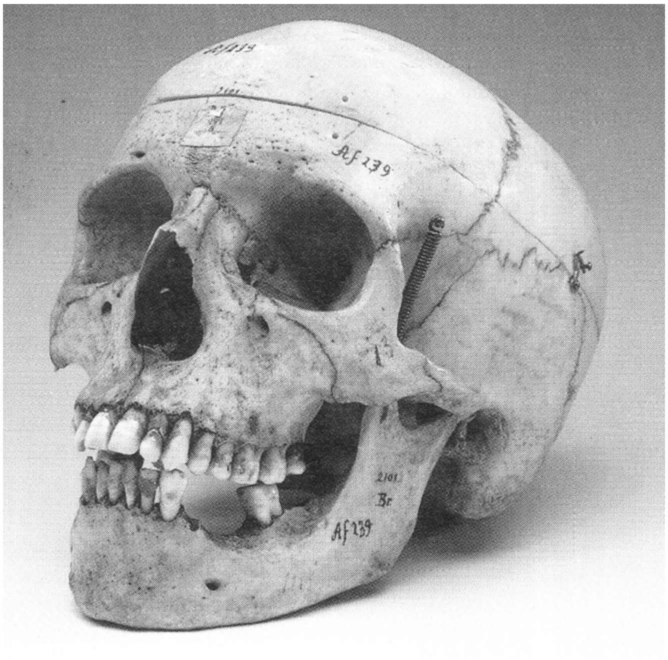

Figure 2.
Skull of a murderer. From the collection of Brugman at the Anatomical Museum in Leiden. Reproduced from "Het vergeten fenomeen Sebald J. Brugman," Museum Boerhaave, Leiden, 2001/2.

their polygamous inclinations. Higher mental functions are located in the upper and frontal regions of the brain, which are lacking in animals. These early public lectures on neuroanatomy were noted down and illustrated by Stuart (1806).

Interest in phrenology was widespread, also among Dutch academic anatomists. Skulls used by S.J. Brugmans (1763-1819), the Leiden professor of natural history in his phrenological studies, can still be found in the Leiden Museum of Anatomy (Brugmans 2001; Fig. 2). Gall's ideas took a long time to die out. Schroeder van der Kolk, the first Dutch microscopist of the brain, of the 19th century, still mentions the possible involvement of the cerebellum in sexual functions in his publications of 1858 and 1859.

Some idea of the state of the knowledge of neuroanatomy in the Netherlands in the early 19th century can be gained from the Dutch translation of Bock's textbook of anatomy (1841). The extensive account of the gross anatomy of the brain and the spinal cord does not differ essentially from today's textbooks. The sections on the histology of nervous tissue are fairly up to date. Valentin's (1836) description of the globular bodies in the grey matter and the ganglia, with their vesicular nucleus and their nucleolus, is cited. Their continuity with the nerve fibres is not mentioned, with the exception of the origin of the grey, 'organic' (unmyelinated) fibres of Remak (1838) from the globules in the sympathetic ganglia. Bell's (1811) discovery of the sensory function of the dorsal and the motor function of the ventral roots is discussed and extended to van Deen's (1838) suggestion that sensory and motor functions can be attributed to the dorsal and ventral white columns of the cord, respectively. Observations on central connections are rare, with the exception of a remark on the decussation of the ventral white columns of the spinal cord, just below the corpora pyramidalia.

J.L.C. Schroeder van der Kolk (1797-1862) was appointed professor of anatomy and physiology at the University of Utrecht in 1826 as the successor to J. Bleuland (1756-1838). He is best known for his institutional reform of psychiatric care in the Netherlands, but he also published and lectured extensively on subjects of general biology, pathological anatomy, philosophy and neurology. His biography and a complete and annotated bibliography are included in van der Esch's thesis (1954). Schroeder van der Kolk published two long papers on the anatomy and the physiology of the spinal cord (1854) and the medulla oblongata (1858, 1859a,b). His ideas on the structure and the function of the central nervous system were published in 1863.

Schroeder van der Kolk's anatomical studies were clearly influenced by van Deen's observations on the physiology of the spinal cord. Van Deen (1805-1869), as his sur-

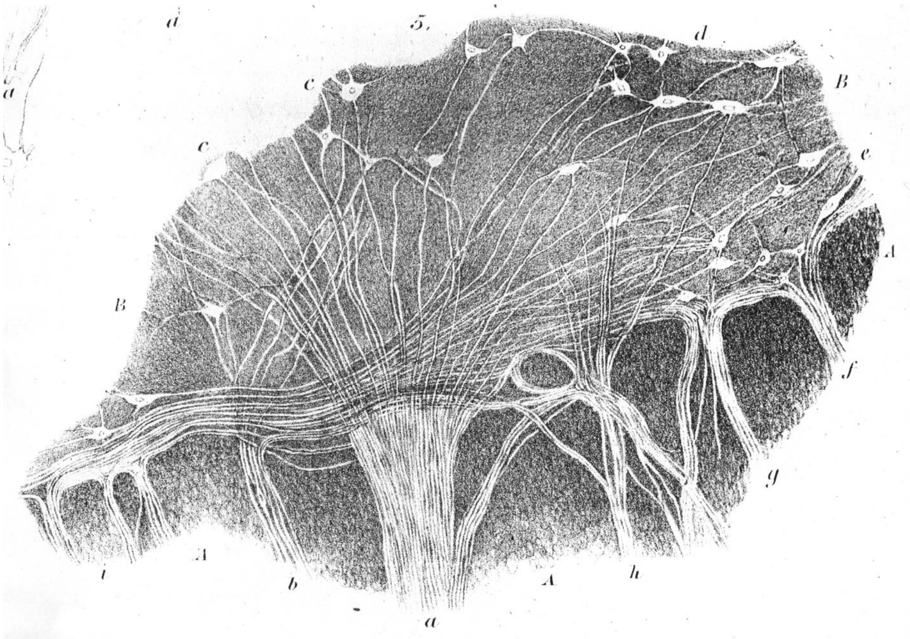

Figure 3.
Section through the anterior horn. Note origin of the ventral root fibres from the anterior horn cells, and anastomosing network of fibres connecting these cells. From Schroeder van der Kolk (1854). Abbreviations: A, white matter; B, grey matter; a,b, two nerve roots for motility, which extend into the grey matter; ccc, multpolar cells, giving origin to nerve roots; d,e, interconnected cells, which receive fibres from the white matter; f,g,h,i, grey ramifications from the horn and the white matter, which continue in cells as in f or constitute a marginal plexus as in i.

name suggests, was of Danish descent. His father was the chief rabbi in Groningen. He studied medicine in Denmark, and later in Leiden, where he received his doctorate in 1834. He practiced medicine in Zwolle, and was appointed professor of physiology at the University of Groningen in 1851. He was a careful observer and a skilled experimenter. He studied the 'nervous circulation', the distribution of reflex movements and strychnine-induced convulsions after partial transections in the cord in eviscerated frogs (van Deen 1838, 1839). He concluded that sensory impressions from the dorsal roots are received by the substantia gelatinosa, and conducted by the posterior white substance to the brain. The anterior white substance subserves voluntary movement. Some of the impressions received by the posterior white columns are not conducted to the brain, but to the substantia spongiosa, the grey matter of the cord. This 'reflex sensation' causes 'reflex movement', conducted by the ventral roots. The substantia spongiosa distributes the reflex-sensation bilaterally. He suggested that the ventral roots take their origin from the substantia spongiosa. His ideas were severely, but unjustly, criticised by Stilling (1842a).

Schroeder van der Kolk used Stilling's method of serial sectioning of ethanol-hardened material, cleared in calcium chlorate. In his papers of 1854 and 1858, Schroeder discusses the origin of the dorsal and ventral roots and the cranial nerves

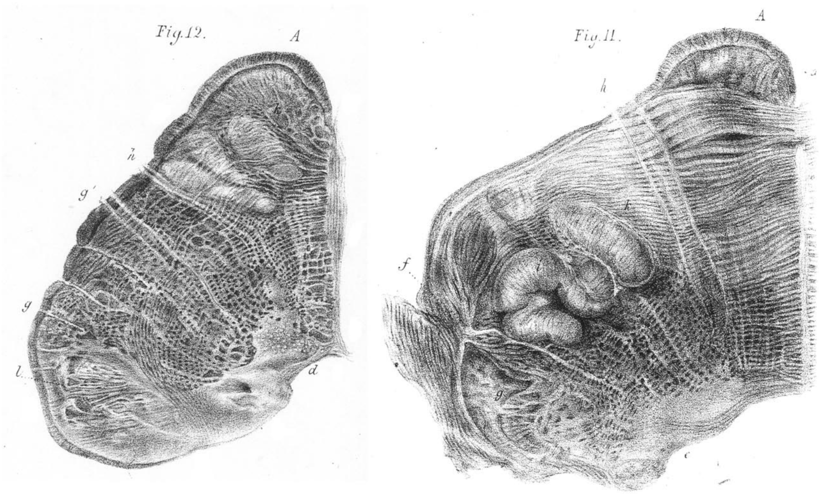

Figure 4.
Sections of the medulla oblongata of the cat, reproduced from Schroeder van der Kolk (1858). Left section taken at the level of the inferior olive, right section at the level of the superior olive. Abbreviations: A, corpora pyramidalia; d, facial nerve nucleus; d, nucleus of the hypoglossal nerve; f, fibrae arciformis; g, root of the trigeminal nerve; h, abducens nerve; h, hypoglossa; nerve; i, corpora olivaria superiores; k, corpora olivaria inferiores (left), superiores (right); l, restiform body.

from the grey matter. He found that the primitive fibres of the ventral root originate from groups of multipolar ganglion cells in the ventral horn, and that similar fibres interconnect these cells (Fig. 3). Dorsal root fibres either pass through the substantia gelatinosa of the dorsal horn as transverse bundles or ascend in the dorsal columns. In the dorsal horn they originate from ganglion cells. The transverse bundles disperse in the grey matter or may continue into the ganglion cells of the ventral horn. The sensory stimuli ultimately reach the thalamus through the dorsal white columns. He observed what later became known as Lissauer's tract (Lissauer 1886), as a layer of small fibres surrounding the dorsal horn, and described and illustrated the marginal cells in this region, later called after Waldeyer (1891).

Originally, Schroeder considered his transverse bundles as reflex fibres that conduct the stimulus to the ganglion cells of the ventral horn, and the ascending fibres as the conductors of sensibility. After he had become acquainted with Brown-Séquard's (1849) observations on hemisection of the cord, he changed his mind and attributed the crossing of sensory impulses at the level of their entrance in the cord to the fibres in the transverse bundles. Longitudinally running fibres in the dorsal horm subserve the coordination of movement; this function, therefore, should not be attributed to the cerebellum.

His account of the decussation of the corpora pyramidalia and their continuity with the ventral columns of the cord, is the same as in Bock's Handbook. These fibres subserve movement of the extremities, and transmit impressions of our volition to the ganglion cells. He does not seem to have been aware of Türck's (1850, 1851a,b) description of the course of the degenerated pyramidal tract in the cerebral peduncle, its partial decussation, and the crossed and uncrossed spinal pyramids. The first complete account of Türck's findings in the Dutch language can be found in Leubuscher (1861). In Schroeder's paper of 1858 the description of descending motor systems is still vague and incomplete. Fibres, descending mainly from the corpora striata, the centres of movement, enter the medulla oblongata, cross in the raphe and carry impressions of our volition to the nuclei of the cranial nerves. The occurrence of a crossed paralysis of the cranial nerves, therefore, is due to the decussation of these descending fibres, and not to a crossed origin of the cranial nerves.

Schroeder van der Kolk was the first to distinguish and to report on the comparative anatomy of the superior and inferior olives (Fig. 4). He considered these nuclei as adjuncts to the cranial nerves passing through them. The inferior olive is concerned with movements of the tongue by the hypoglossal and accessory nerves; in man, where it is extremely large, it is involved in speech.

Cornelis Winkler and his contemporaries: the late 1800s

W. Koster (1834-1907) succeeded Schroeder van der Kolk as professor of Anatomy, but his neuroanatomical studies lacked unequivocal follow-up. No publications by Dutch authors on neuroanatomical subjects appeared between 1860 and 1880 and I have been unable to find any Dutch textbooks discussing the great developments in neuroanatomy in this period.

Cornelis Winkler (1855-1941) acknowledged Donders' brilliant lectures on physiology and Donders' influence on his own later career (Winkler 1947). It was in the lab of Donders' son-in-law, Professor Th.W. Engelmann (1843-1909), who had taken over Donders' lectures in histology in 1866, that Winkler, still a student, started his research. His interest in neuroanatomy was awakened some years later when, as an assistant in internal medicine, he spent his free time repeating Fritsch and Hitzig's (1870) demonstration that electrical stimulation of the cerebral cortex induced motor responses in C.A. Pekelharing's laboratory(1848-1922). During tours of German psychiatric institutes, which he made at Donders' suggestion before his appointment as a lecturer in psychiatry in 1885, he met von Gudden, Meynert, Obersteiner, Edinger and Weigert. On his return to Utrecht, he started experiments on rabbits, using von Gudden's method of secondary atrophy, but he did not publish on this subject at that time.

During his lectureship and his later professorship of Neurology and Psychiatry in Utrecht (1893-1896) he published only a few anatomical papers on the origin of the pyramidal tract (1885, Winkler and Wellenbergh 1986), which he (mistakenly) located in posterior central gyrus and the lobulus paracentralis, and on the localisation of fibres from more posterior parietal and temporal regions in the lateral portion of the cerebral peduncle (1886). After his appointment as professor of neurology and psychiatry in Amsterdam (1896-1914), most of his publications were still concerned with

Figure 5.
Winkler's lab in Utrecht in the early 1920s: Verhaart (1), Freule van As van Wijck (2), mevr. Winkler-Junius (3), Ada Potter (4), Winkler (5), Stenvers (6), de Ruiter (7), C.G.M. de Vos (8), ? (9), Koopmans (10), mej. Hoogland (11). Courtesy of ir. P. Verhaart.

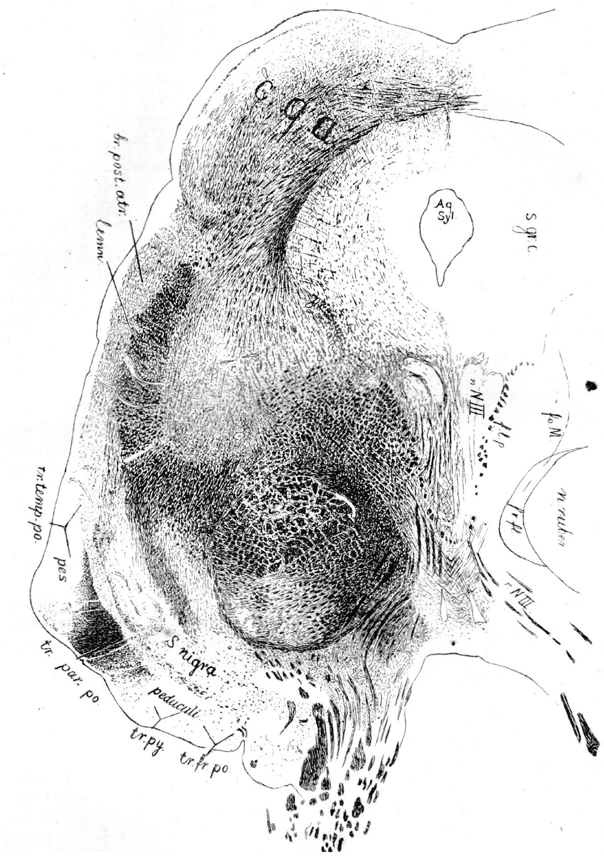

Figure 6.
Weigert-stained section through the mesencephalon, of a case with a large softening of the cerebral hemisphere. Drawing by Ada Potter, legends in Winkler's handwriting. Winkler, Handbook (1920).

clinical or forensic subjects and matters of organisation. One of his main anatomical interests during this period was the anatomy of the eighth nerve. In a lengthy treatise (1907) he described the partial overlap in the distribution of the vestibular and cochlear nerves, and was able to follow their fibres, across the midline, in what was already known at the time as the secondary vestibular and cochlear pathways (Fig. 14). These observations were confirmed in the thesis of Valeton (1907) on the myelination of the vestibulo-cochlear nerve and in the second volume of Winkler's *Handbook of Neurology* (1917-1933). The observations by Cajal (1899) and others on the absence of overlap and the more limited termination of these nerves were apparently not taken into consideration by Winkler.

Experimental anatomical and physiological studies on the vestibular system were also conducted by L.J.J. Muskens (1872-1937), another of Winkler's pupils, who received his doctorate shortly after Winkler had left Utrecht in 1896. Muskens practiced neurology and neurosurgery in Amsterdam. He is best known for his demonstration of the 'ascending tract of Deiters' (1913), the uncrossed ascending connection of the vestibular nuclei, which has nothing to do with Deiters' nucleus, and which still plays a controversial role in conjugated horizontal eye movements (Baker and Highstein 1978). His scientific life's work was summarised in a monograph of 1935.

The numerous students who obtained a doctorate under Winkler's guidance are listed in his Opera Omnia (1918). During this period he also started his collaboration with Ada Potter, whose anatomical atlas of the rabbit brain (Potter 1911) was published as her thesis. Her skill in drawing produced the *Anatomical guide to experimental researches on the cat's brain* (Winkler and Potter 1914), the unfinished atlas of the human brain (Winkler and Potter 1930), and many of the illustrations in Winkler's later publications. The cat atlas was the first publication to be supported by the Remmert Adriaan Laan Foundation, one of Winkler's creations, which still supports the publication of neuroanatomical research. The human atlas was part of an international project, inspired by the Brain Commission, of which only some of the large-scale drawings of Fuse and von Monakow (1916-1929) were realised in the Zürich Brain institute.

Winkler moved back to the Utrecht in 1915 (Fig. 5). In the period up to his retirement in 1925 he wrote the last three volumes of his *Textbook on Neurology* (1917-1933) and supervised the theses of Bok (1922), Hoeneveld (1923), Verhaart (1925) and others. His textbook is an impressive monument to his knowledge of neuroanatomy, but as a reference book it is almost useless. Winkler acknowledged the contributions of others, but without dates or references. Descriptions and Ada Potter's illustrations of histological preparations of the brain of man or animals, unpublished experiments of unknown provenance and diagrams, all labelled in his own handwriting, are combined into a very personal, five volume account of neuroanatomy (Fig. 6). I doubt whether many of the neurologists and psychiatrists, to whom these volumes were addressed, ever read them.

Winkler, who spent much of his time behind the microscope, according to his own testimony and to that of his biographers (Brouwer 1942), was foremost a teacher, a clinician and an influential and well-connected organiser. He started, together with L. Bolk, the short-lived Dutch journal for anatomy *Petrus Camper* (1901-1905), he founded the Society of Amsterdam Neurologists together with C.T. van Valkenburg, K.H. Bouman and J.K.A. Wertheim-Salomonson in 1909, and was one of the three initiators of the foundation of the Central Institute of Brain Research in Amsterdam in the same year. Through his students, Verhaart and Bok, most of today's neuroanatomists are his second or third generation successors (Table II). Winkler's collection of histological slides is kept at the Netherlands Institute of Brain Research in Amsterdam.

During the last decades of the 19th century, three other Dutch anatomists, Eugène (M.E.F.T) Dubois (1858-1940), G. Jelgersma (1859-1942) and W.H. Cox (1861-1933) started their research: Dubois in the Department of Anatomy in Amsterdam; Jelgersma and Cox as house doctors in asylums for the insane. None of them had had a gymnasium education when they entered medical school and, as a consequence of the legislation of the time, they were not admitted to a doctorate. This was remedied by the conferral of honorary doctorates to Dubois by the University of Amsterdam in 1897, and to Jelgersma and Cox by the University of Utrecht in 1896. L. Bolk, the future professor of Amsterdam, who did not even finish the gymnasium, received an honorary degree from Leiden in 1902.

Eugene Dubois is best known for his discovery of the fossiled remains of the Pithecanthropus erectus in Trinil on the Indonesian island of Java between 1890 and 1892. Before that time, he started publishing on the relationship of brain weight to body size (Dubois 1897a,b; for later publication see Brummelkamp 1937). He distinguished two exponents that determine this relationship. The somatic exponent determines the relationship of brain size with body weight in a group of animals whose brains are of a similar organisational level. Dubois found that the value of this exponent of 5/9 was very similar for mammals of quite different orders. The cephalisation factor determines the 'psychic', i.e., organisational level of the brain. For the human brain the cephalisation factor was calculated at 2.81, for the antropoid apes at 0.75, for the mouse at 0.0779, and for the shrew at 0.0688. These studies were pursued later by several of C.U. Ariëns Kappers' students. Brummelkamp's thesis (1937) applied the theory of cephalisation to anthropological problems, which interested Ariëns Kappers during the later part of his career. Dubois and Brummelkamp concluded that the increase of the encephalisation factor from more primitive orders to the primates is a saltatory one, following an arithmatic progression. More recently the subject was reviewed, and Dubois' and Brummelkamp's ideas were criticised by Hofman (1982) and van Dongen (1998). Dubois' approach can be recognised in Bok's mathematical description of the structure and the progressive development of the cerebral cortex , which will be considered in the next section of this chapter.

Jelgersma was still a student when he was appointed prosector at Meerenberg (Carp 1942). Jelgersma was a prolific author: he published more than 50 papers, many of them on neuroanatomy before his appointment as a professor of Psychiatry in Leiden, in 1899. His writings were occasionally lacking on carefully researched anatomical detail, but they often contained interesting analogies and original ideas on functional correlations. From circa 1910 onwards his main interest went out to psychoanalysis. After his retirement in 1930, he published his well-known *Atlas anatomicum cerebri humani* (1931), which later appeared in Ranson and Clarke's (1959). His original research on the internal structure of the brain of aquatic mammals was published as a monograph in 1934. His collection of histological preparations is still kept at the Department of Physiology of Leiden University (Marani et al. 1987).

Jelgersma made important contributions to the functional anatomy of the cerebellum, the first time in 1886, in a series of publications in international journals (see Carp 1942 for references) and in two monographs (1904, 1920). He conceived the cerebellum as reciprocally connected with the cerebral cortex through the cerebello-thalamic and cortico-ponto-cerebellar systems, and with the periphery, through the spinocerebellar tracts and the descending limb of the superior cerebellar peduncle, which he, mistakenly, supposed to terminate in the spinal cord. Afferent fibres from the pons terminate as mossy fibres in the cerebellar cortex and influence Purkinje cells through the parallel fibres, the axons of the granule cells. Climbing fibres, therefore, are the terminals of another pathway, i.e., of the spinocerebellar tracts that relay peripheral stimuli to the Purkinje cells. The cerebellum coordinates simple reflex movements or automatisms (low-level coordination) and learned, compound movements such as locomotion and speech, which involve the cerebral cortex (high-level coordination). Coordination is achieved by the Purkinje cells, the central elements of the cerebellar cortex, which project to the cerebellar nuclei, the source of the efferent pathways of the cerebellum. When a movement is initiated by the cerebral cortex, the

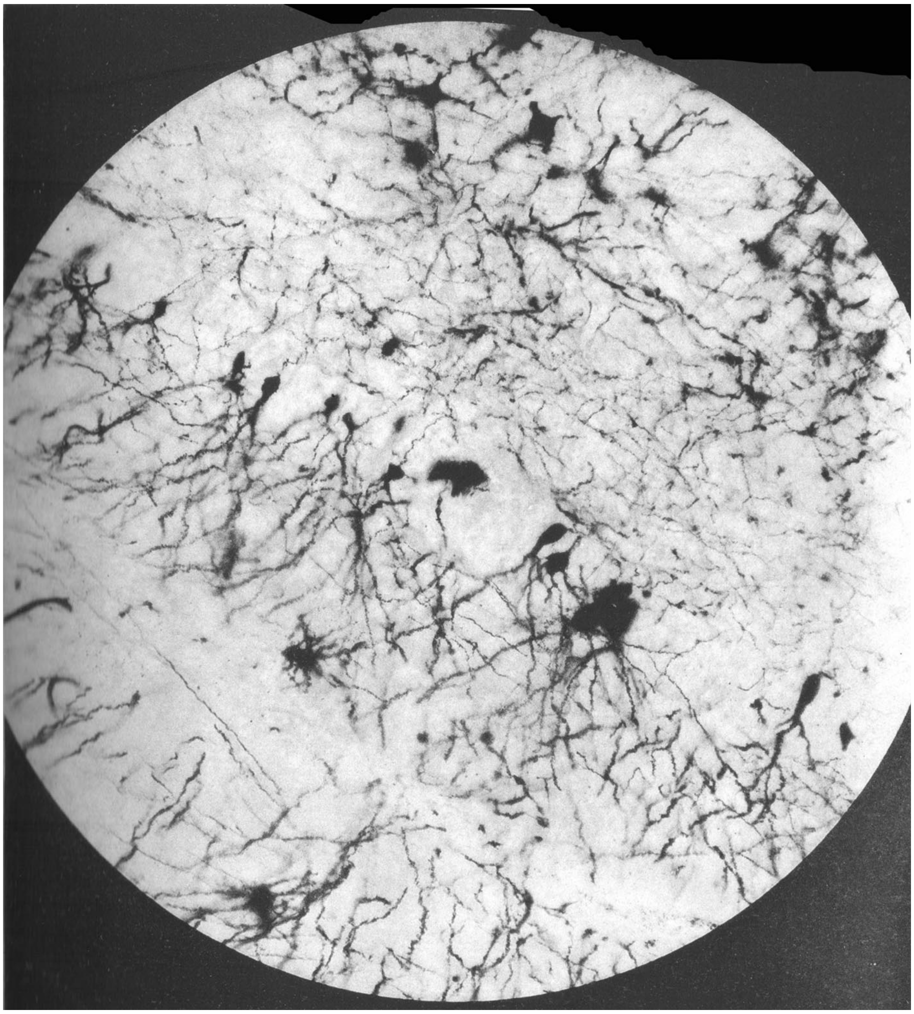

Figure 7.
Golgi-Cox section of the fascia dentata. From Cox (1891).

Purkinje cells receive a representation of the movement from the cerebral cortex, through the mossy fibre-parallel fibre pathway and an image of the actual movement through the climbing fibres from the periphery. When the two images match, the movement is correct, when there is a mismatch the Purkinje cells send a corrective stimulus to the periphery.

Recently, my attention was drawn to Jelgersma's publication on *Connections* (*Schakelingen*) from 1928, where he postulates the formation of new, temporary connections in the brain in the learning process involved in higher forms of coordination. Jelgersma's ideas on the function of the Purkinje cells and the role of plasticity in cerebellar coordination, therefore, predate the modern, and very similar concepts on long-term adaptation of movement by the Purkinje cells of the cerebellum (Marr 1969, Ito 1982).

From 1888, W.H. Cox worked in Brinkgreve, a psychiatric hospital in Deventer. In a short paper (Cox 1891) he published the protocol for his well-known modification of the Golgi method (Fig. 7). Although the 'Golgi-Cox' method has been and still is used by many others, I have been unable to find any publications showing Cox using it himself. His interest in neuroanatomy was apparently short-lived. After 1898 he only published on clinical, organisational and moral matters.

Anatomy reborn: the early decades of the 20th century and the interbellum

Winkler, Dubois and Jelgersma continued their studies during this period, but new trends were set by Louis Bolk, who was appointed professor of anatomy at the University of Amsterdam in 1898. The Central Institute for Brain research in Amsterdam was opened in 1909, with C.U. Ariëns Kappers as its first director, and the careers of the self-made neurohistologist J. Boeke and of four of Winkler's pupils, J.W. Langelaan, B. Brouwer, W.J.C. Verhaart and S.T. Bok developed during this period.

The ascent of Louis (Lodewijk) Bolk (1866-1930) to the chair of Anatomy in Amsterdam

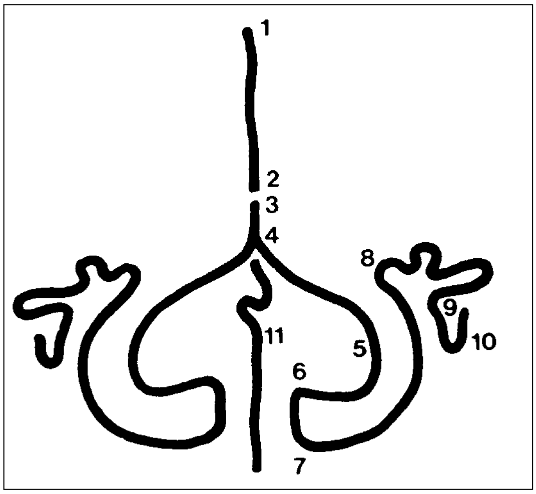

Figure 8.
Wire diagram of the subdivision of the mammalian cerebellum by Bolk (1906). Behind the undivided anterior lobe (1-2) and the lobulus simplex (3-4), the cerebellum divides into the folial chains of the vermis (11) and the hemisphere. The hemisphere can be subdivided into the ansiform lobule (5), the paramedian lobule (6-7), the crus circumcludens (8-9: the present paraflocculus) and the uncus terminalis (10, the flocculus).

in 1898 was as rapid – he had received his medical degree just two years before – as it was unexpected. The board of the University had recommended the appointment of the residing lecturer, the German Seidel, and had named Eugène Dubois as a second, but the city council of Amsterdam decided otherwise (Baljet 1992). Bolk was a typical gross anatomist, using observation and dissection as the only tools in his research (reviewed in van Limborgh and Nieuwenhuys 1975). What distinguished Bolk was the innovative, sometimes provocative quality of his concepts and generalisations. This is well illustrated in his address on 'Brain and Culture' on the occasion of the anniversary of the University of Amsterdam in 1918, published in 1932. According to Bolk, the superior weight of the human brain cannot be explained as a consequence of functional adaptation or selection, but should be understood as the fixation of the high fetal brain/body ratio in the human species. This was the first mention of his well-known retardation or fetalisation theory (reviewed by Dullemeijer 1975).

Bolk acquired a well-deserved place in neuroanatomy through his studies of the comparative anatomy of the mammalian cerebellum (Bolk 1906; reviewed by Voogd 1975, and Glickstein and Voogd 1995). Bolk applied his generalized 'blueprint' of the mammalian cerebellum in his theory on functional localisation (1903, 1906, 1908). The fact that later investigations failed to substantiate this theory did much to discredit Bolk's work. His nomenclature, however, has survived (Fig. 8) and his ideas on the morphology of the cerebellum have proved to be of fundamental importance in the understanding of the basic longitudinal subdivision of this organ in more recent times (Voogd and Glickstein 1998).

In 1915, Bolk started up annual meetings of Dutch anatomists in his new department at the Mauritskade in Amsterdam. In 1930, these meetings led to the foundation of the Dutch Association of Anatomists. His students later occupied most of the chairs of anatomy in Holland (Fig. 9: A.J.P. van den Broek, Utrecht; J.A. Barge, Leiden; M.W. Woerdeman, Amsterdam) and the Dutch East Indies (W.A. Mijsberg, Batavia).

Together with Winkler, Bolk was instrumental in the foundation of the Central Institute for Brain Research. In 1901 the German anatomist and neuroembryologist Wilhelm His took the initiative for a proposal of the 'Königlich Sächsische Gesellschaft der Wissenschaften' to the recently founded International Association of Scientific Academies at their meeting in Paris, to stimulate international collaboration in neuroscience. This resulted in the formation of the 'Brain Commission', with representatives from existing brain institutes in the U.S.A, Spain, Switzerland, Russia and Germany. The Brain Commission made plans for an international division of labour in neuroscience, and stimulated the foundation of brain research institutes in other countries. Winkler and Bolk, in an official report accepted by the Royal Academy of Science, proposed the foundation of a Brain Institute in Amsterdam, although Jelgersma informed the Academy that a Brain Institute could be accommodated in his quarters in Oegstgeest, and that, in his opinion, addition of a single technician would suffice (Ariëns Kappers 2001). Winkler and Bolk's plans were adopted. The city of Amsterdam built a new accommodation for the Brain Institute, next to the new Department of Anatomy on the Mauritskade and on Tuesday June 8, 1909 the new institute was opened by Professor J.D. van der Waals on behalf of the Royal Academy, in the presence of Golgi, von Monakow and other members of the Brain Commission with addresses by Winkler, Waldeyer and the newly appointed director, C.U. Ariëns Kappers (van der Waals 1909). It turned out to be the last act of the Brain Commission, it fell apart with the outbreak of the Great War, and its good intentions were left to slumber until the foundation of the IBRO (International Brain Organisation) by the UNESCO in 1960.

As a medical student C.U. Ariëns Kappers (1877-1946) worked on neuranatomical subjects in the laboratories of Winkler and of J. van Rees, the professor of histology in Amsterdam, and the supervisor of his thesis (Ariëns Kappers 1904, 1906), which was based on studies of the brain of fishes and started in the Zoological Station in Napels in 1901. In 1906 he joined Edinger in the Senckenbergisches Institute in

Figure 9.
Painting by Martin Monnickendam of the 'Anatomical lesson of professor Louis Bolk'. Bolk is sitting in the middle, dissecting an orang-utan. Barge is looking over his shoulder; Boeke is depicted on the left and van den Broek on the right. The painting probably commemorates the publication of the Dutch textbook Anatomy by van den Broek, Boeke and Barge in 1925 (Baljet 1993). From the collection of the University Museum Amsterdam. Photography: Gert Jan van Rooy.

Frankfurt. The collaboration with Edinger probably decided his future career in comparative neuroanatomy (Ariëns Kappers 1915). It was here that he first published on the possible explanation of phylogenetic differences in position of the cranial motor nuclei, as yet without using the term 'neurobiotaxis' (Ariëns Kappers 1907).

The Central Institute for Brain Research, where he was appointed as director in 1908, counted two neurologists among its staff: C.T. van Valkenburg (see the chapter in this book) as assistant-director and E. de Vries (1883-1976). Although anatomical and neuropathological studies on the human brain appeared from their hands, the main theme of the Brain Institute remained the comparative anatomy of the central nervous system until Ariëns Kappers' retirement and death in 1946. Ariëns Kappers only became an Extraordinarius of Neuroanatomy at the University of Amsterdam in 1929. Before that time the students he supervised obtained their Ph.D. from his professorial colleagues (i.e., van der Horst 1916, and Schepman 1918, both with professor Sluiter in Amsterdam, Kooy with van Wijhe in Groningen)

The career and the personality of C.U. Ariëns Kappers are discussed in chapter 16. His autobiographical notes, which have been published recently (Ariëns Kappers 2001), give some interesting sidelights about his life. Van Valkenburg's and de Vries's anatomical contributions are considered in chapters 27 and 9, respectively. The interesting career of Ae.B. Droogleever Fortuyn, one of Ariëns Kappers early collaborators, started with a thesis on the cytoarchitecture of the mouse (1911). Droogleever wrote the first volume on the central nervous system of non-vertebrates (Ariëns Kappers and Droogleever Fortuyn 1920). He became a lecturer in Histology in Leiden, and later took on a professorship at Peking Union College. His last anatomical publications date from this period (1934). At the outbreak of the war he moved to the Americas, to become connected to the medical school in Paramaribo (Surinam). In later years he only published on genetics.

According to Nieuwenhuys (Nieuwenhuys et al. 1998) "The research of Ariëns Kappers and his numerous associates was almost exclusively based on non-experimental material, stained with the Weigert-Pal method to stain myelinated fibres and counterstained with paracarmine for cell bodies. [...] The works by Ariëns Kappers and his allies (1920/21, 1936, 1947) may be (considered as) attempts at reconstructing the phylogenetic history of the central nervous system of vertebrates. It is important that in these works this history is presented as a progressive process, thought to be driven by an undetermined, intrinsic force .... The results of this entelechic tendency [...] are seen in the progressive development of the brain in accordance with a general plan, in the progressive differentiation and adjustment of its constituents, and in their mutual general relations" (Ariëns Kappers et al. 1936). Ariëns Kappers' theory of neurobiotaxis is an attempt at inferring generalisations from observed differences between the brains of vertebrates (Ariëns Kappers 1907, 1908, 1911, 1919, 1928). According to this theory, simultaneous and successive stimulations from a certain source extert a neurotropic action on neurons, and are responsible for their position near the source of these stimuli. Nieuwenhuys (1998) points out how this theory was extrapolated into a law of association, which governed the presumed migrations of neuronal populations in many parts of the brain. Such an ordering principle, certainly, was needed to bring some order in the enormous number of observations on the central nervous system of vertebrates, documented in the publications from the Central Institute of Brain Research.

J.W. Langelaan (1871-1963) completed his thesis on muscle tone with Winkler, in 1900. He became a professor of Anatomy in Leiden in 1903, but left again in 1909 (Fig. 10). Heringa (1963) recorded his remark "I came to Leiden to learn about the anatomy of the nervous system; once I knew it, I left." He published on the development of the cerebral commissures (1908a) and the human cerebellum (1908b, 1919). He wrote one of the finest Dutch textbooks on neuroanatomy (1910). It contains an extensive, introductory review of the development of the brain, and is superbly illustrated by the medical artist, G. Koster (Fig. 11). In his later career, Langelaan returned to his neurological practice and to his physiological and microscopic studies of striated muscle in the labs of Boeke and Heringa. He became a member of the Royal Academy in 1929. His model of muscle contraction and his studies on the innervation of striated muscle have been disproved by later developments.

Figure 10. Portrait of J.W. Langelaan (1871-1963), probably taken around 1910. Courtesy of the Department of Anatomy and Embryology, University of Leiden.

After a fairly undistinguished thesis on the acoustic system in a case of congenital deafness, supervised by Winkler (Brouwer 1909), which surprisingly earned him a Cum Laude (with honours) (see chapter 19), B. Brouwer (1881-1949) developed into one of the first Dutch experimental neuroanatomists. He became acquainted with the use of secondary degeneration in the tracing of neural pathways, through the studies on the topical projection of the retina on the tectum opticum in fish by P.C. Zeeman, the Amsterdam professor of Opthalmology, and J. Lubsen (Lubsen 1921) in the Central Institute of Brain Research. Although Ariëns Kappers was opposed to the use of animals in experimental research, he did not impose this conviction on his students.

Brouwer succeeded van Valkenburg as assistant-director of the Brain Institute and later was appointed as a professor of Neurology in Amsterdam in 1923. He was invited to deliver the Herter lectures in Johns Hopkins in Baltimore in 1926 (Brouwer 1927). His tours of the United States, and his ensuing correspondence with John Fulton, were the subject of recent papers by Koehler and Bruyn (2001) and Koehler (in press). During the years of the Second World War, Brouwer acted as Rector of the University of Amsterdam. He succeeded Ariëns Kappers as director of the Central Institute of Brain Research in 1946 and died in 1949.

In his first Herter lecture, Brouwer summarised his experimental studies of the connections of the optic nerve in rabbits, cats and primates (1923, 1930; Brouwer and Zeeman 1926; Overbosch 1927; Fig. 12). Brouwer took off where K.H. Bouman had left off, studying the anatomy of the visual system in one of the first studies using the Marchi

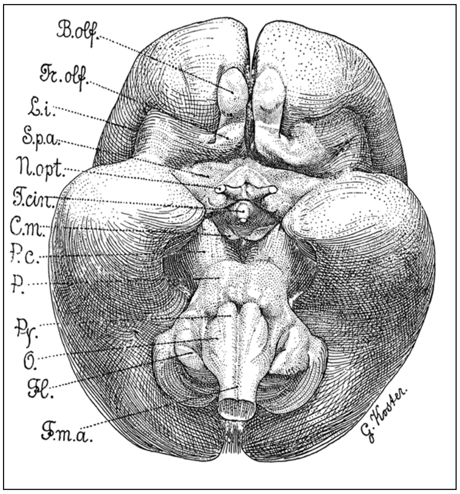

Figure 11.
Ventral view of the brain of a human fetus at the end of the fifth month of gestation. Drawing by G. Koster. From Langelaan (1910).

method in this country (Bouman 1905). Thalamo-cortical connections were studied by two of Brouwer's students, F.E. Posthumus Meyjes (1932) and J. Droogleever Fortuyn (1938). Droogleever Fortuyn's thesis, especially, remains a readable, authoritative account, which discusses his experiments on the thalamo-cortical projection in the rabbit, against the background of the new contributions of Le Gros Clark, Mc Rioch and Walker on the subdivision and connections of the thalamus of that period. Droogleever Fortuyn (1906-1999) became a professor of Neurology in Groningen in 1950. Centrifugal connections of the visual cortex were charted in the thesis of Biemond (1929). A. Biemond (1902-1993) succeeded Brouwer on the chair of Neurology in Amsterdam.

Another subject raised by Brouwer in his Herter lectures (Brouwer 1927) was the subdivision of the cerebellum. This was a hot topic at the time, debated among the proponents of Edinger's (1910) original distinction of a palaeo- and neocerebellum, adepts of Bolks's ideas on functional localisation in the cerebellum, and the adherents of van Hoeneveld's (1923) intussusception of 'neocerebellar', afferents in palaeocerebellar territory. Van Valkenburg (1913) studied corticogenesis in human fetus. He found that Purkinje cells, between the fourth and seventh month of gestation, replace the outer layer of the internal granular lamina. This change occurs earlier in Edinger's palaeocerebellum, than in the neocerebellum. In more recent publications on this subject it was shown that Purkinje cells are already present in the cortex, long before granule cells settle in the internal granular layer, and that regional differences in corticogenesis occur between multiple, longitudinal zones in vermis and hemisphere, rather than between palaeo- and neo-cerebellar subdivisions (Korneliussen 1968). Hoeneveld described a case of olivo-ponto-cerebellar atrophy. His concept of 'intussusception' is based on the premise that the neo-cerebellar nuclei of the pons and the inferior olive are a source of mossy fibres. From the partial preservation of the myelinated mossy fibre plexus in the granular layer in the vermis and portions of the hemisphere, he concluded that neocerebellar territory has become intercalated in the palaeocerebellum. For the distribution of mossy fibres Hoeneveld's conclusion is correct, although his methods are questionable. For the inferior olive, which turned out to be the exclusive source of the climbing fibres only much later (Desclin 1974), Brouwer showed that it incorporates both neo- and palaeocerebellar parts, confirming earlier observations of Holmes and Stewart (1908).

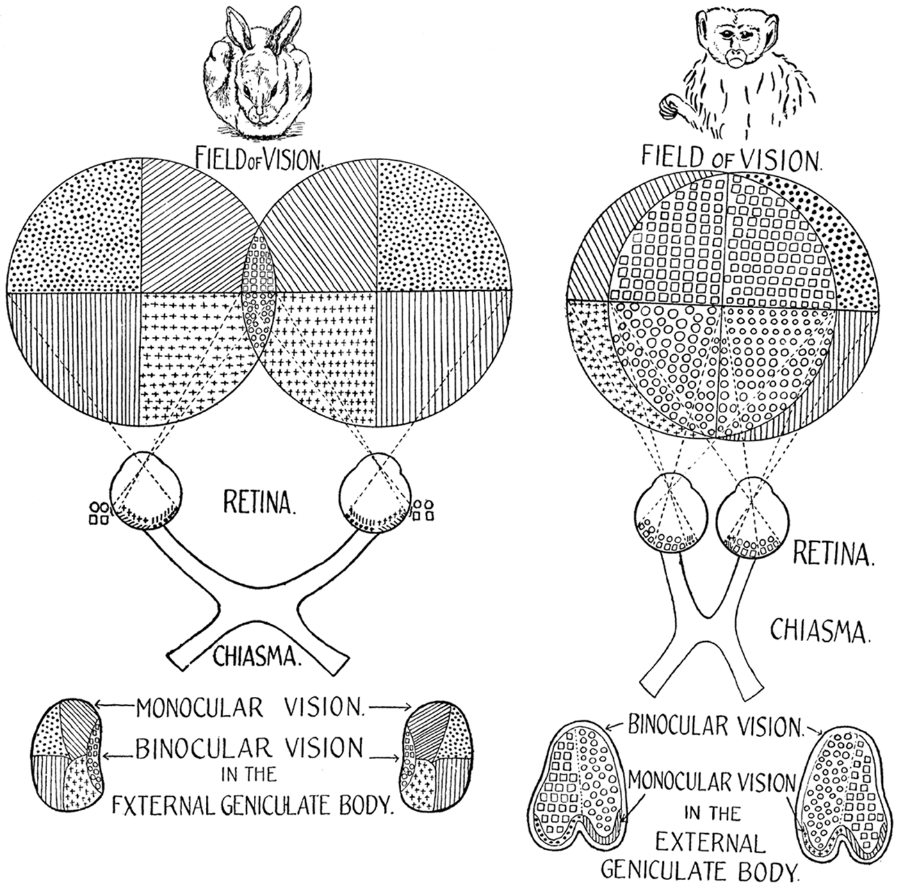

Figure 12.
Projection of the visual fields in mammals with laterally-positioned and with frontal eyes. From Brouwer's Herter Lectures (1927).

In human cases of 'neocerebellar' atrophy, which spared the vermis and the flocculus, Brouwer found an intact rostromedial dentate, with the medial and interposed nuclei, and demyelination of the caudolateral dentate, which, apparently, received a projection from the atrophied neocerebellum (1913, 1915, 1919, 1921; Brouwer and Coenen 1919, 1921). Some years later Gans (1924) discovered a similar division of the human dentate nucleus, on the basis of its iron content. A. Gans (1885-1971) was another of Winkler's students, who became a lecturer in Neurology at the University of Leiden.

S.T. Bok (1892-1964) wrote a thesis supervised by Winkler (Bok 1922), worked for some time as a neuropathologist in the Valerius clinic with professor L. Bouman, and was appointed as a professor of Histology and Microscopical Anatomy in Leiden in 1929. From 1953 till his retirement in 1962 he was director of the Central Institute for Brain Research in Amsterdam.

His thesis is a systematic analysis of the early development of the neuronal connections in the spinal cord in the chicken embryo, culminating in a general blueprint of the cord. Bok devised the theory of stimulogenic fibrillation to explain the position of the different elements in his blueprint (Bok 1915a,b; Fig. 13). This blueprint also served as the basis for his chapter on the spinal cord in Von Möllendorff's *Handbook* (1928). One element of this blueprint, the localisation in the dorsal columns, was elaborated in the important thesis of Lietaert Peerbolte (1932). Bok later applied this plan to higher levels of the central nervous system (Bok 1926). Although these generalisations, combined with Bok's selective use of the literature, sometimes lead to absurd conclusions, his approach had a great didactic value. His lectures, which I attended in the early 1950s (Bok et al. 1951; Fig. 14), were superb.

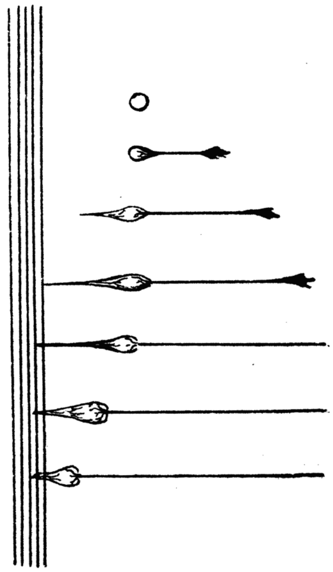

Figure 13.
Diagram of the outgrowth of axon and dendrites, perpendicular to the fibre system from which the neuron receives its stimuli. From the paper of Bok (1915a,b) on the theory of stimulogenic stimulation.

Bok's interest in the quantification of the nervous system, started with his paper on the influence of the gyration of the hemisphere on cortical thickness (1929a,b). Together with his student van Erp Taalman Kip, Bok resumed Dubois' approach in his studies on factors determinating thickness and area of the cerebral cortex (Bok 1934, van Erp Taalman Kip 1938). Renes (1940) found a constant density of fibres in the cortex, and stated that they are separated by a constant distance, determined by the vacuolisation of the cortical protoplasm. In 1959, Bok reported that these vacuoles may be identified as the site of memory. Although Bok's research was handicapped by his strong convictions and generalisations, his introduction of statistical and stereological methods in neuroanatomy has been of lasting significance (J. Ariëns Kappers 1964a,b). In the Central Institute of Brain Research his approach to the quantification of the cortex was followed by Colon (1968), G.J. Smit (1968) and H.B.M. Uylings (1977), who initiated new studies on the quantitative histology, the ontogenesis and the areal subdivision of the cerebral cortex.

The saddest story of this period is that of the fate of the neuron theory on the Dutch scene. C.A. Pekelharing, the successor of Edelmann as professor of Histology in Utrecht, gave a lucid account of the history and the status of this theory at the outset of the 20th century, in his *Lectures on Histology* (1905). He emphasised the indisputable support for the neuron theory drawn from observations with the Golgi and the Ehrlich methylene method, which never revealed anything like Gerlach's (or Schroeder van der Kolk's) anastomosing dendritic network, or Golgi's axonal reticu-

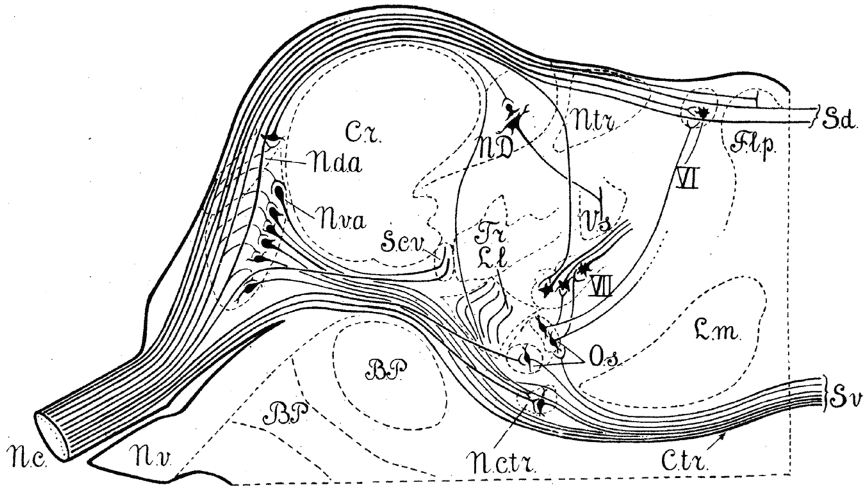

Figure 14.
Diagram of the termination of the cochlear nerve, redrawn by G. Koster for Langelaan's (1910) textbook, from Winkler's (1907) experimental study of the vestibulo-cochlear nerve. In addition to the terminations in the dorsal (N.d.a.) and ventral cochlear nucleus (N.d.v.), Winkler found cochlear root fibres in the dorsal acoustic striae, dorsal to the restiform body (C.r.) and in the corpus trapezoides (Ctr). Although it was well known at the time that these connections do not exist, the Figure was still reproduced by Bok in 1951.

lum of anastomosing axons. He pointed out that the arguments against the neuron theory stemmed from the observations of Apathy and Bethe of a neurofibrillar network, extending uninterruptedly from one neuron to the next. Cajal negated these observations with his own, new reduced silver methods, which showed that neurofibrils always remain confined within a single neuron. However, his opponents, using gold-toning, were able to demonstrate the continuity of the neurofibrils with an intercellular network.

In the Netherlands, J. Boeke (1874-1956) and his student G.C. Heringa (1891 – 1972) were among the most vehement opponents of the neuron theory. Boeke completed a thesis on a pharmacological subject with the Amsterdam physiologist Laplace in 1901. On a visit to the marine biological institute in Naples in the same year, Boeke met Apathy, with whom he spent four months working in his lab in Kolasvar, Hungary (Heringa 1961). In 1905 he became lecturer in Histology, and in 1909 professor of Anatomy in Leiden, as the successor of Langelaan. From 1919 till 1946 he occupied the chair of Histologyand Embryology in Utrecht, as the successor of Pekelharing. During his long academic career, Boeke received numerous scientific honours, medals, memberships of learned societies and four honorary degrees.

Using his own modifications of the Bielschowsky method, Boeke showed the continuity of the neurofibrils in the motor end plate with a periterminal net extending into the sarcoplasm (Boeke 1911). Similar observations were made by Heringa in his thesis of 1916 (Fig. 15) on the developing sensory corpuscles of Grandry and Herbst in the duck bill, where neurofibrils of the nerve fibre could be followed into a lighter-stained proplasmatic neural network extending into the entire corpuscle,. Heringa later occupied the chair of Histology in Amsterdam from 1920 until 1960. Akkeringa, another of Boeke's students, observed the presence of a periterminal network in the retina (Akkeringa 1934). In the theses of Boeke's students van Esveld (1927) and Leeuwe (1937), the periterminal net was described as a neural syncytium connecting the ganglion cells and the interstitial cells of the gut. Boeke discovered a double innervation of striated muscle by motor endplates and sympathetic fibres (Boeke 1911, 1934), for which he received the Wilhelm Roux medal in 1934. In his studies on the development or the regeneration of peripheral nerves, Boeke again denied the developmental unity of the nerve cell. Growing axons incorporate protoplasm of a syncitium, consisting of epithelial, mesodermic and muscle cells. Anastomosing neurofibrils from different nerve cells populate the resulting neural network (Boeke 1916).

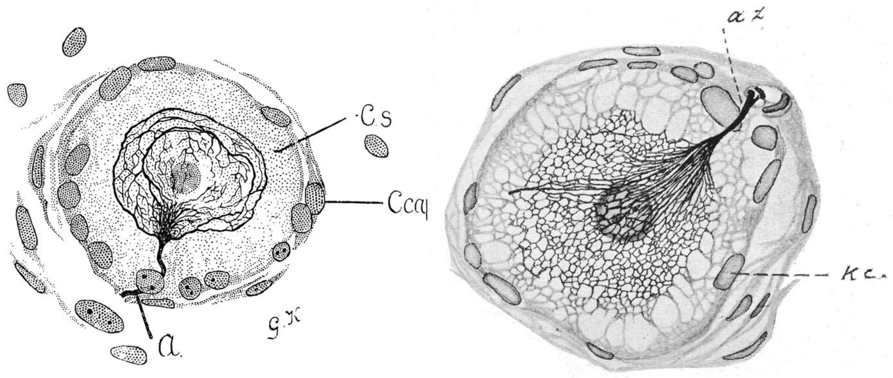

Figure 15.
Drawings of sensory corpuscles of Grandry in the duck bill. The left-hand drawing is by G. Koster from Langelaan (1910), based on a Cajal silver preparation from E. van der Velde (1907), showing a well-demarcated fibre plexus in the centre of the corpuscle. The right-hand drawing is from Heringa (1916). It shows how the central, neurofibrillar plexus merges with the lighter-stained 'terminal net' of Boeke, which permeates the entire corpuscle.

In their textbook (Boeke, de Groodt and Heringa 1939) and their publications, Boeke and Heringa clearly and repeatedly stated their position: "It is well known ... how rapidly the first enthusiasm (for the concept of strictly individual cell units) cooled. The Golgi-forms of the central nervous system appeared to offer – in the long term – no true foundation of the neuron theory" (Heringa 1923); and "Only we feel every time more strongly, how far and irretrievably we are separated nowadays from the old simplistic conceptions of the neuron theory of the former century..." (Boeke 1934). Cajal honoured them with a sharp reprieve in his last monograph, *Neurinismo o reticularismo*, which appeared shortly after his death, in 1933. Cajal convincingly showed that observations on a periterminal net depend on the vagaries of the staining methods, and remarks how "The discovery of the Dutch authors has been welcomed by Held," one of Cajal's chief opponents, "who reproduced the figures of these authors with belated delight." Held was not the only one, Langelaan (1910), Winkler (1912) and Ariëns Kappers (1938) all shared some of Boeke's convictions.

Heringa and Boeke were men of principles. Boeke resigned from the (then no longer Royal) Dutch Academy of Sciences when all Jewish members were expelled in 1941. Heringa was removed from his chair and interned by the German occupants (Ariëns Kappers 2001). In a publication of 1949 Boeke took his stand for the last time. He died in 1956, two years after the demonstration by Palade and Palay (1950) of the discontinuity of nerve cells in the synapse under the electron microscope. When Heringa evaluated Boeke's scientific work in 1961, he still hesitated to answer the question whether Boeke's life's work had become worthless, in the affirmative. Strangely, Heringa never mentioned his own responsibility for the lost battle against the neuron theory.

The apogee: the post-war era

On November 18, 1945 W.J.H. Nauta (1916-1994) defended his thesis on the role of the hypothalamus in sleep-regulation, in Utrecht, a few months after the Dutch universities had reopened and tried to overcome the ravages of the war. Nauta had started his research on the anatomy of the hypothalamus in 1937 as a medical student, shortly before the outbreak of the Second World War, with a group of scientists, led by J. Dankmeyer (1907-1973), the future professor of Anatomy in Leiden (Dankmeijer and Nauta 1941, Nauta 1941). His first paper on his quest for silver impregnation of degenerating axoplasm dates from this period (Dankmeyer and Nauta 1939). After the University of Leiden had been closed by the Nazi authorities in 1941 (for being a "hornet's nest of ideological subversion"), Nauta moved to Utrecht, where he received his medical degree, and where he worked at the anatomical laboratory of A.J.P van den Broek (Schmitt 1995). He returned to Leiden, but soon accepted a position in Anatomy with Professor G. Töndury in Zürich in 1947. In collaboration with the Swiss chemist P.A. Gygax he published on silver impregnation of degenerated axons with a modification of the Bielschowsky silver method (Nauta 1950, Nauta and Gygax 1951). The suppression of normal axons with oxidation by permanganate, at the favour of the silverimpregnation of the degenerated axons, was discovered in collaboration with another scientist, L. Ryan, and the 'suppressive method' was published in its final form with Gygax (Nauta and Ryan 1952, Nauta and Gygax 1954, Nauta 1993). The Nauta method

Figure 16. Walle J.H. Nauta. 1916-1994.Courtesy of the M.I.T. Museum, Cambridge, Massachusetts, USA.

revolutionised tract tracing, and fomented numerous papers on connections within the central nervous system, from every part of the world for the next two decennia. In 1951 Nauta moved to the newly founded Division of Neuropsychiatry at the Walter Reed Army Institute of Research in Washington. In 1955 he was appointed to a professorship at the University of Maryland and in 1964 he joined the Department of Brain and Cognitive Sciences at the Massachusetts Institute of Technology (M.I.T.) in Cambridge as a professor of Neuroanatomy, where he received the title of Institute Professor, the highest professorial rank given by the M.I.T., in 1973 (Fig. 16).

In the Walter Reed and the M.I.T. he founded an influential school of neuroanatomists, which included W.R.H. Mehler, H.G.J.M. Kuypers, L. Heimer, H.J. Karten, Ann Graybiel and Patricia S. Goldman-Rakic. He never returned to the Netherlands, but the postdocs of the Dutch neuroanatomists H.T.M. Lohman and H.J. Groenewegen, who spent some time with Nauta in the M.I.T., created a lasting bond. Nauta published extensively on the hypothalamus and limbic system (1969, 1986/6), the connections of the frontal lobe (1971), striatum and cerebellum (Mehler and Nauta 1974), and on comparative anatomical topics (Nauta and Karten 1970). His Friday lectures on neuroanatomy were an institution attended by students and local Nobel Prize winners alike.

Dankmeijer's group of students of the hypothalamus fostered other neuroscientists. One of them was H.J. Lammers (1921-1994). Lammers completed his Ph.D. with Barge and became the first professor of Anatomy at the new medical school of the Catholic University of Nijmegen in 1951. Here he was joined by A.H.M. Lohman, a lecturer in Anatomy in Nijmegen, and a professor of Anatomy of the Vrije Universiteit in Amsterdam from 1977 until 1995 (Smeets and Groenewegen 1995). Studies of the hypothalamus and the limbic system were pursued by Lammers (Gastaut and Lammers 1961). Lohman mainly published on the olfactory system (Lohman 1963). In the group founded by Lohman in Amsterdam, the limbic system has remained one of the main research topics, in the investigations of the 'limbic' striatum of professor H.J. Groenewegen (Groenewegen et al. 1997), and the combined anatomical, electrophysiological and imaging studies of professor M.P. Witter (Room and Witter 1985, Rombouts et al. 1999). P.G.M. Luiten, another of Lohman's students (Luiten 1977), became a professor of Zoology at the University of Groningen, where he founded a research group that made important contributions to the anatomy of memory (van der Zee and Luiten 1999).

H.G.J.M. Kuypers (1925-1989) wrote his Ph.D. thesis with Bok in Leiden, on the connections of the central grey, where he used Nauta's 1950, non-suppressive silver technique (Kuypers 1952). He aborted his residency in Neurology, with J. Droogleever Fortuyn in Groningen, when Nauta invited him in 1955 to join his group at the University of Maryland at Baltimore (see Moll's chapter and Lemon 1990). In 1962 he moved to a full professorship at Western Reserve University, Cleveland, Ohio. Kuypers applied the suppressive Nauta method in his classical studies of the medial and lateral components of the motor system in cats and primates, where he combined anatomy with observations on motor behaviour (Kuypers 1962). In 1966 he returned to the Netherlands as the founding professor of Anatomy at the Erasmus

University Rotterdam. Here he continued his interdisciplinary studies, with the neurologists and physiologists D. Lawrence, S. Miller and R. Lemon, who received appointments as lecturers or professors in his department (Godschalk et al. 1981, Holstege and Kuypers 1982, Lawrence and Kuypers 1968). It was here that he developed new retrograde double labelling techniques, using fluorescent tracers (Huisman et al. 1982). In 1985 Kuypers moved to Cambridge, where he studied the use of viruses as transneuronal tracers, together with Gabriella Ugolini and P. Strick (Kuypers et al. 1989; Kuypers and Ugolini 1990). He became a Fellow of the Royal Society in 1988. He died, suddenly, in 1989. In the Netherlands, G. Holstege continued Kuypers' anatomical approach, as a professor of Anatomy in Groningen, adding a third, 'emotional motor system' to Kuypers' earlier medial and lateral systems (Holstege 1990).

Dankmeijer's hand can also be seen in the appointment of W.J.C. Verhaart (1898-1983) as the successor of Bok in the chair of MicroscopicalAnatomy in Leiden in 1953. Verhaart's scientific career, as a student of Winkler, is told in another chapter of this book. In the case of Verhaart, the introduction of another histological method, the Häggqvist-modification of the Alzheimer-Mann method, changed the face of the microscopical topography of the brain. In his lab, the apportioning of different parts of the brain to different students, left the cerebellum as my research object on my arrival as a student. These cerebellar studies were continued during my appointment as a lecturer in Leiden (1978) and as the successor of Kuypers in the chair of Anatomy at the Erasmus University Rotterdam (1985-1998). Electron microscopy of the nervous system was introduced in Leiden by G.F.J.M. Vrensen in the Anatomical Laboratory of 'Endegeest' in Oegstgeest, under the directorship of J. Stotijn. Vrensen made important contributions to the stereology of synapses (Vrensen and de Groot 1973, Vrensen et al. 1980). In the Department of Zoology in Leiden, J.L. Dubbeldam (1968) and G.A. Zweers (1971) initiated neuroanatomical and behavioral studies in birds, in close collaboration with Verhaart. Verhaart's neuroanatomical laboatory was incorporated later in the Neuroregulation group, in the Department of Neurosurgery, under E. Marani. In Rotterdam the borders between the disciplines became erased, when the old Departments of Anatomy and Physiology merged in the new Department of Neuroscience, under Voogd's successor, professor Chr. de Zeeuw, in 2002.

Under the directorship of Bok, from 1953 till his retirement in 1962, the Central Institute of Brain Research moved from its cramped quarters at the Mauritskade, to the more spacious, but still temporary, barracks at the Ydijk in Amsterdam. Electrophysiology, ethology and neurochemistry made their entrance. Comparative neuroanatomy was resumed by R. Nieuwenhuys; the Golgi method was re-introduced in the research of H. van der Loos. J. Ariëns Kappers succeeded Bok as director of the Brain Institute in 1962. His interest in the autonomic nervous system was fostered by his uncle, C.U. Ariëns Kappers, but J. Ariëns Kappers focussed his research on the epiphysis cerebri. In 1975 Kappers' student, the neuroendocrinologist D.F. Swaab, took over his directorship. He supervised the move of the Institute to a new building, an annex of the Amsterdam Medical Centre. Swaab's studies of gender-related specialisations in the hypothalamus (Swaab et al. 1995), and of sustained activity on the fate of neurons ("use it or lose it," Swaab 1991) received considerable interest. Under his directorship the scope of neuro-morphology was considerably broadened.

R. Nieuwenhuys left the Brain Institute to take up a position as professor of Morphology of the Nervous System in Nijmegen, in 1967 (Nicholson and Smeets 1992). Like C.U. Ariëns Kappers, most of his studies were done on normal material, but in his case the scope of these studies was broadened by the introduction of histochemical and immunohistochemical techniques (Nieuwenhuys 1985). His student H. Steinbusch was the first to prepare antibodies against catecholamines (Steinbusch et al. 1978). Steinbusch was appointed later as a professor of Neuroscience in Maastricht. Extensive experimental studies on lower vertebrates were undertaken by Nieuwenhuys's student, H.J. ten Donkelaar. The comparative studies on the morphogenesis and anatomy of the nervous system by Nieuwenhuys and his students have been collected recently in the three volumes *Central Nervous System of Vertebrates* (Nieuwenhuys et al. 1998). Nieuwenhuys retired in 1992. His vacant chair was never reoccupied, and reorganisation by the Medical Faculty in Nijmegen decimated his former research group, putting an end to almost one hundred years of research in the comparative neuroanatomy in The Netherlands.

The re-introduction by H. van der Loos (1929-1993; Fig. 17) of the Golgi method in Dutch research and his appreciation of the historical roots of the neuron theory (van der Loos 1987) restored some of the harm done by Boeke and Heringa during the first half of the 20th century. His thesis on dendro-dendritic relations from 1959, based on observations with the Golgi-Cox method, as yet without electron-microscopy, traces the history of these connections and attempts to quantify these 'ephapses' in the cerebral cortex of the rabbit. In 1960, van der Loos joined David Bodian's group at the Johns Hopkins Medical School in Baltimore, where he was appointed full professor in 1971. He became a Senior Research Scholar of the Kennedy Foundation after his knowledge of brain development was brought to the attention of the family of John F. Kennedy (Molliver and Welker 1994). In 1973 he became director of the Institut d'Anatomie of the University of Lausanne. From the large body of his publications, his paper on the discovery, with Tom Woolsey, of the representation of the facial whiskers in the barrel-area in the sensory cortex of the mouse (Woolsey and van der Loos 1970) stands out as the beginning of a new and productive line of research in neuroscience. Van der Loos was a gifted and charismatic speaker, his lectures were carefully rehearsed acts, presented with the skill of a born actor. The sudden death of this great Dutch neuroanatomist in 1993 shocked the neuroscience community throughout the world.

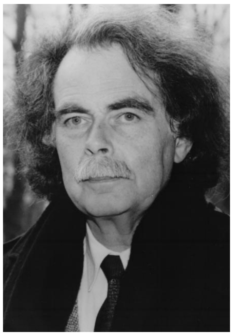

Figure 17.
H. van der Loos. 1929-1993.Courtesy of Prof. E. Welker, Department of Anatomy, University of Lausanne, Switzerland.

Neuroanatomists are dependent on their technicians for most of their material. A few of their names have been provided: Kouw, Jelgersma's technician, Winkler's technicians, Mrs. E. Winkler- Junius, Winkler's second wife, and Miss Hoogland (Fig. 5), and J. Langhout, T. Brouwer and C. Roosemeyer (Brouwer et al. 1919) from the crew of C.U. Ariëns Kappers. More than anything, neuroanatomical publications are dependent on the quality of their illustrations. C. Koster, Langelaan's illustrator, Ada Potter, Winkler's alter ego, Chr. Vlassopoullos. Ariëns Kappers illustrator from 1915 until 1936, Jan Tinkelenberg, the versatile Leiden medical artist and Chr. Van Huijzen, who illustrated much of Nieuwenhuys's work, deserve much of the credit for their patrons' publications.

Today's position of neuroanatomy in neuroscience research and in the medical curriculum has changed. Neuroscience research has become an interdisciplinary effort, where molecular biology and physiology, and clinical applied imaging of the brain, play the upper hand. Classical neuroanatomy and the study of the chemoarchitecture and the ultrastructure of the brain remain indispensable, but as an independent (and predominantly male) discipline neuroanatomy is about to become part of the history of science.

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Neuropathology 9

G.W. Bruyn and J.L.J.M. Teepen

The vicissitudes of neuropathology in the Netherlands during the past century do not offer a cheerful story if compared with the course of its events abroad. Located at the crossroads between England and Germany, France and Scandinavia, the Low Countries are subject to marked influences from its neighbours. Dutch Neuropathology was dominated by German influence during the period circa 1880-1940 and became completely oriented towards Anglo-Saxon science after 1945.

Within the framework of the present chapter one does not need to go into detail about the birth and growth of neuropathology during the nineteenth century. The present authors assume the reader to be sufficiently cognizant of it and, if not, will have access to ample documentation on the subject (see reference list). Suffice it to recall that in England John Abercrombie (1781-1844; the founding father of neuropathology there) and his contemporaries John Cheyne (1777-1836), Matthew Baillie (1761-1823), Robert Hooper (1773-1835), Richard Bright (1789-1859) and their successors Sir Robert Carswell (1793-1857) and James Hope (1801-1841) set the stage of morbid anatomy of the nervous system for the introduction of the microscope on a large scale. In France, after the pioneering histologist Xavier Bichèt (1771-1802), it was Jean Cruveilhier (1791-1873) and J.M. Charcot (1825-1893) and pupils who initiated neuropathology. In Germany, Rudolf Virchow's (1821-1902) cellular pathology paradigm set the crown upon the work of Matthias Jacob Schleiden (1804-1865) and Christian Gottfried Ehrenberg (1795-1876). It released an avalanche of impressive German neuropathological studies by a mere twenty to thirty psychiatrists and neurologists – from Wilhelm Heinrich Erb (1840-1921) and Carl Otto Westphal (1833-1890) to Walther Spielmeyer (1879-1935) and Hugo Spatz (1888-1969) – which was to perpetuate Germany's leading role in neuropathology well into the second half of the twentieth century.

In fact, the discipline of neuropathology was created and developed by a relatively small band of psychiatrists and neurologists, dedicated to a Holy Grail-like ideal: searching and finding the neural cause of mental as well as of neurological disease. Its stages from embryology via adolescence to senescence were guided and nurtured by these men (and women) of neuropsychiatric signature in Europe; the input from general pathologists long remained quasi non-existent which, after all, is curious. The process closely parallels what happened with neuro-radiology, a field in which practically all methods invented and results obtained (from myelography to encephalography, to angiography, to CT-scanning; the Californian neurologist William Oldendorf invented the method synchronously with G.N. Hounsfield, but the last-named received knighthood as well as the Nobel Prize, which caused quite some indignation in the USA neurological circles) were the work of neurologists. Since the final quarter of the previous century, the discipline has been annexed by the specialty of radiology.

Factors, or rather entire fields of empirically-won knowledge, that formed the conditions *sine qua non* for the amazing surge of neuropathology are summarised in Spielmeyer's concise booklet (1914) and the small monographs by Bertrand and by Stam. They include: the art of fixation of neural tissues (such as chromic acid, later ethanol, formol or osmium tetroxyde); the proper way of embedding blocks (celloidin, paraffin); the techniques to obtain (serial) slices of certain thickness and sizes (from hand-held razor-blades to von Gudden's first microtome to modern machines); the perfection of staining the slices for which such pioneers as Weigert, Golgi, Gerlach, Ramon y Cajal, Ehrlich laid the basis, as the hematoxylin-eosin stain intrinsically lacks the potency to bring out the components of neural cells and fibres; and, of course, the physical sophistication that developed the single-stage microscope to the multistage apparatus with Abbe's condensor, achromatic flat-field lenses, light-filters, Zernike's phase-contrast, etc.

Add to this the fact that the nervous system shows specific reactions to adverse influences (to mention only Vogt's pathoclisis, retrograde/transneuronal/Wallenberg/system-degenerations, Nissl's 'primary Reizung', Schollen-formation, etc.) unlike reactions in other tissues. Generally speaking, in pathology, it scarcely makes any difference whether a specimen of bone, lung or liver is examined at a few millimetres or even a few centimetres from another such specimen with respect to cell-type, cell-size, cell-reaction, or remote effects; it certainly does so in the CNS. The *métier* of interpreting changes in organs differs profoundly from that of a complex system.

When the early giants in neuropathology had largely done their work, the succeeding generation's *feu sacré* flagged somewhat between the nineteen twenties and thirties *grosso modo*. Then, World War II broke out, and a moratorium on neuropathological activities ensued. About a decade (1945- 1955) post-war, when the ravages of the war had been cleared away and Europe had been rebuilt, with most thanks due to the Marshall Plan, an intriguing phenomenon unfolded: the revival of neuropathology, both of its organisational aspects – to which we will refer below – and its technical enhancement due to the larger scale introduction of electron microscopy, cyto-/histo-/enzyme chemistry, and specific antibody immune analysis, pushing the frontiers substantially beyond those of the 'old' neuropathology.

The developments of neuropathology in the Netherlands largely mirrored those prevailing in Germany during the first half of the century. Autonomic chairs of Neurology began to be created rather late (Amsterdam, the first, in 1923) and more often than not disposed of clinical facilities in their 'own' building – denoted as the 'pavilion-system' – as well as their 'own' neuropath laboratory. In view of the events from about 1980 onwards, it is almost ironic to note that the first 'Extraordinariate in Neuropathology' (in connection with psychiatry) was established in Amsterdam as early as 1861, a position occupied by the psychiatrist G.E. Voorhelm Schneevoogt (1814-1871). The close relationship between psychiatry and neuropathology in those times, founded in the concept that the key to open the door to understand and cure mental disease was held by brain research, was emphasised at the University of Utrecht, which appointed the anatomist/psychiatrist J.C. Schroeder van der Kolk whose attempts to find the cause of epilepsy by exploring the *pons cerebri* under the microscope remained in vain.

Just after the *fin de siècle*, the psychiatrist W.H. Cox (1862-1929), a brilliant though somewhat bellicose man, who, at the time, worked in the mental institute 'Brinkreve'(Deventer), greatly improved Golgi's silver-stain method. He was awarded a doctorate *honoris causa* by the University of Utrecht in addition to gaining eponymic recognition (the 'Golgi-Cox stain'). His father-in-law, the Utrecht ophthalmologist H. Snellen (1834-1908), is also of eponymic fame for his invention of charts to measure visual acuity. In this early period, to mention another example, the Professor of Psychiatry G. Jelgersma, whose anatomical merits tower above his meagre psychiatric performances when he – temporarily – left the path of scientific rectitude and had a fling with psychoanalysis, was the first to identify marked atrophy of the caudate nucleus in Huntington's chorea at a German medical congress in Cologne (1908). Though Anglade had noticed this atrophy two years earlier, in 1906, it was Jelgersma, who essentially opened up the road to neuropathological study of basal ganglia diseases.

On screening the *Psychiatrische en Neurologische Bladen* (renamed *Folia*, and *PNN* and *CNN*) between 1897 and 1985, one notices some 130 clinical-pathological observations, written by some 40 neuropsychiatric colleagues. With rare exceptions, one cannot discern a systematic thread running through the rather heterogeneous motley of reports, nor a focus of research. Most are anecdotes, covering almost the entire spectrum of neurological nosology. This reflects the two ways in which neuropathology can be practiced: a) to pose a definite diagnosis which confirms (or contradicts) the clinician and defines the site and nature of the causative lesion, or b) to clarify scientifically a certain causal or pathogenetic neuropathological process, thus bringing the art to a higher level of sophistication. Even at the moment of writing, form (a) predominates practically everywhere, because it is easier.

If the above-mentioned 130 reports are arranged according to their author(s), one observes that a few colleagues showed an inclination to restrict their studies to a particular topic.

Winkler's spouse, Mrs. M.E.C. Winkler-Junius, repeatedly published on glia- and Hortega cells; V.W.D. Schenk, initially psychiatrist of the 'Maasoord-Portugaal' mental hospital and later neuropathologist of the Rotterdam Medical School, focused on Pick's dementia; B. Brouwer (Amsterdam) studied 'degenerative' diseases and was among the very first to define late cortical cerebellar atrophy as a remote effect of malignancy; the neurologist-neuroanatomist W.J.C. Verhaart (Batavia, Leiden), repeatedly reported on demyelinating disease, CNS malformations, the substrate of dementia in mongoloid idiocy and reported the first case of what today goes by the name of multiple system atrophy; Ernst de Vries, in a certain sense the father of neuropathology in the Netherlands after his return from Batavia in 1948, consistently studied astrocyte-reactions and presented convincing evidence for two types of postvaccinial (perivenous) encephalitis at the International Congress of Neuropathology, London, 1955. This modest, lean, ascetic man of a small build and of sparse, softly spoken words, son of the famous Hugo de Vries of the mutation-theory, started out as a psychiatrist. He then worked in the Central Brain Institute (Amsterdam) from where he published on the development of the claustrum and neostriatum, went to lecture on neurology in Leiden, followed by many years in Peking as associate professor, subsequently as professor in Batavia's Medical Faculty, finally to head the neuropathology laboratory in the Neurology Department at Utrecht. Drawing on a vast experience, he was a keen microscopist. One of the present writers, a pupil of his, saw him change the erroneous diagnosis of schizophrenia to the correct one of pellagra, on noticing the typical Betz' cell changes at first glance. In a baffling clinical case of encephalitis, he posed the correct diagnosis of chronic myeloid leukaemia on noticing the contents of a small pontine artery occluded by stasis, confirmed later by general autopsy.

Gans, lecturer Neurology in Leiden between 1923 and 1925, wrote a number of papers on a senile dementia in which he found cerebral atrophy remaining exclusively restricted to the frontal lobes, irrespective of arterial supply territories, and with a hereditary transmission. He coined the eponym 'Pick's atrophy' for this uniquely frontal atrophy. Since then, the eponym 'Gans syndrome' entered the literature (Pryse-Phillips 1995).

The trend to focus one's neuropathological studies intensified after the late 1950s. In the Valerius Kliniek (Vrije Universiteit, Amsterdam), F.C. Stam concentrated on leukodystrophies and, together with J.M. Wigboldus, on dementias. He described an unknown form of dementia that he called 'racemose' dementia because of the grape-bunch-like deposits of sialomucoprotein. Clinically, the case was compatible with the diagnosis of Creutzfeldt-Jacob disease, but neuropathologically clearly something else. Should it be denoted as 'tam's dementia'? In retrospect, one might suspect the case to have been one of adult polyglucosan body dementia but that diagnosis does not fit at all. Stam et al. (1980) also described another rare dementia, as a separate form of Lafora disease. Furthermore, Stam published a *Compendium of Neuropathology*. Together with Dick Swaab of the Central Brain Institute, Stam founded the 'Brain Bank' in 1985, a highly successful venture that serves neuropathological research throughout the world, and which served, in our country, as matrix for, for example, Kremer's new findings on the tuberomamillary and lateral tuberal nuclei in Huntington's chorea, Parkinson's disease and Alzheimer's dementia as well as Swaab's revolutionary findings of changes in certain hypothalamic nuclei in sexual differentiation and in Alzheimer's dementia (1988-1992). In the Utrecht neuropathology lab, A. van Rossum (succeeding de Vries) focused on extrapyramidal disease, and F.J.M. Jennekens specialised in neuropathies and myopathies. Frans Jennekens originated the enclosed fibre-type method for type-grouping in myosin ATP-ase stained muscle sections; he discovered a shift towards type 1 fibres plus reinnervation with progressing age, particularly in legmuscles.

The laboratory of the Neurology Department of the Wilhelmina Gasthuis (Municipal University, Amsterdam) enabled A. Biemond to define hereditary posterior column ataxia ('Biemond's Ataxia') as well as 'Biemond syndrome III' (autosomal recessive congenital analgesia). W.A. den Hartog Jager, together with J. Bethlem, signalled the sphingomyelin-constituent of Lewy bodies, the involvement of the adrenals in Parkinson's disease, and, over a decade, together with J.M.B.V. de Jong, studied spinal motoneuron reactions to changes in the diet of experimental animals in an attempt to pinpoint the metabolic cause of ALS. Jaap Bethlem reorganised the work in the lab so as to gear it to the study of myopathies. This resulted, in close collaboration with George K. van Wijngaarden, in a steady flow of high-quality papers, including one that gave rise to the eponym 'Bethlem's disease'. One of the present authors, who worked in Bethlem's lab for a year in 1963, received a warning from him that the microscopic techniques are always lurking to fool the observer: late 1962 he had noticed rod-like structures in the myocytes of a puzzling case, but discarded them as fixation or staining-artefacts because a literature check did not come up with anything like it; a year later, Milton Shy et al. described the rods in what is hence known as nemaline myopathy. David Moffie published a regular stream of neuropathological observations from the Amsterdam Alma.

The lab in the Leiden neurological department was used initially for the work-up of (heterogeneous) clinical material. After the arrival of G.T.A.M. Bots, who had trained in neuropathology at McGill's in Montreal, the lab's activities were focused on CSF-cytology, Creutzfeldt-Jakob disease, Huntington's chorea and hereditary cerebral amyloid disease. G.W. Bruyn et al. defined the neuropathology in hereditary spastic dystonia cum Leber's hereditary optic neuropathy due to a mutation in the mitochondrial genoma at np 14596.

Following the 1960s, Nijmegen's Institute of Neurology welcomed H.J. Slooff (pathologist) who had trained abroad to specialise in CNS tumours. The Nijmegen group of Gabreëls, child-neurologist, was most productive in the study of metabolic myopathies (and neuropathies) forming a reference centre for many hospitals abroad. His wife, A.W.M. Gabreëls-Festen, consistently studied hereditary neuropathies, defining the autosomal-recessive demyelinating type of Charcot-Marie-Tooth disease, histopathologically characterised by basal lamina onion bulbs, the causative mutation which was found by her group seven years later.

In Rotterdam the neurologist-pathologist S. Stefanko took neuropathology under his wings with the exception of the domain of muscle diseases that remained the province of Verhaart's pupil, the neurologist H.F.M. Busch.

Bethlem's initiative clearly found fertile soil in our country for the study of myopathies, witness the various 'muscle-centres' that have arisen over the past few decades in Amsterdam, Utrecht, Rotterdam, Leiden and Nijmegen. Unfortunately, we cannot say whether any specific neuropathological spearhead research is being done in Groningen. As there was only limited time to prepare the present chapter, a full in-depth inventory was not possible; a quick scan research had to suffice.

In order to complete a fair and balanced survey, one of us composed a fairly exhaustive list of neuropathological papers written or co-authored by Dutch pathologists. Because the primary material underlying them, i.e., biopsy or autopsy material from patients in neuroclinical wards, is usually part and parcel of specific topics of neurological interest, their co-authorships substantially outweigh first authorships. The same applies even to papers on rare, new or baffling clinical observations; this reflects the distinction – made above – between (routine) clinical and focused, in other words, experimental neuropathology.

The collection comprises some 800 papers written by between 15 and 20 pathologists. A minority of the papers was published in journals of neuropathology or of general pathology. Almost all of them appeared after the late 1970s or early 1980s. This testifies to the relatively recently awakened interest of pathologists for neuropathology, perhaps fostered by the then imminent 'Decade of the Brain'. It also reflects the historical change in the Dutch landscape, where a once exclusively neurological province is being progressively colonized and taken over by pathologists, a change as necessary as inevitable in our modern times of ultra-advanced techniques.

The collection did not contain the circa 500 papers by Prof. D.F. Swaab of the Central Brain Institute, because of the lack of time. We limited ourselves to an abbreviated sketch of topics repeatedly (co-)authored by the pathologists during the period 1980-2000, and refrained from evaluating the merits of the papers in the collection.

University of Amsterdam:
Prof. D. Troost: temporal lobe epilepsy; gliomas; ALS and AIDS.
Vrije Universiteit Amsterdam:
W. Kamphorst: dementias, M.S.
P.H. van der Valk: M.S.
J.M. Roozemuller-Kwakkel: Alzheimer; microglia.
Leiden:
Prof. G.T.A.M. Bots: CSF-cytology; CNS amyloid; viral encephalitides.
M. Maat-Schieman: medulloblastoma; Huntington's chorea; CNS amyloid.
Sj. van Duinen: myopathies; CNS-amyloid.
Utrecht:
G.H. Jansen (recently left for Canada): prionoses; hippocampal epilepsy.
Groningen:
W.F. den Dunnen: nerve regeneration.
Rotterdam:
Prof. S. Stefanko (retired in 1999): CNS malignancies.
J.H. Kros: oligodendroglioma.
Nijmegen:
Prof. J.L. Slooff: CNS malignancies; encephalitides.
Dr. M. Lammens: (nemaline) myopathy; CNS-malformations.
P. Wesseling: CNS-malformations and malignancies.
Enschede:
R.A. de Vos: Parkinson; Alzheimer; supranuclear palsy.
Tilburg:
J.L.J.M. Teepen: critical illness neuropathy; neuro-oncology.

This list shows that neuropathologists today explore gliomas (genetics and growth-factors; Van der Valk, Troost), oligodendroglioma (features, variants, basics; Kros), vascular growth in gliomas (Wesseling), prionoses (Jansen), hereditary disease (Leiden), neurodegenerations (de Vos, Kamphorst) and congenital brain-/muscle-disorders (Lammens).

To conclude, we turn to the organisational aspects of neuropathology in the Netherlands as well as abroad in order to give the overview more background. We referred above to a revival in neuropathology about one decade after the Second World War. This revival apparently expressed an increasingly felt need to strengthen the professional ties, to emphasise the specific identity of the field, and to organise neuropathology in a formal, statutory body on the basis of the concept of an autonomous speciality. Bailey's paper of 1964 and Ferraro's paper of 1954 indicate, that the USA pioneered the development toward a separate neuropathology discipline. From the original 'Neuropathologists Club', formed in 1924, the 'American Association of Neuropathology' was born in 1934. With characteristic push, the American neuropathologists founded the *Journal of Neuropathology and Experimental Neurology* in 1941. In those days, the Association counted nearly 100 members, federal funding of training programmes in three centres and exams had been obtained, and the well-known J. Godwin Greenfield came every year to the N.I.H.-Bethesda centre to give tuition and training. By 1964, the USA already boasted 20 training centres. Support and input from neurology was considered to be of substantial value. Among those trained, the number of neurologists was considerable. As early as 1959, an American Certificate of Neuropathology was available to physicians who had the Pathology Board diploma plus an additional two years training in neuropathology. The neuropathologist A. Ferraro initiated the – now impressive – series of International Congresses of Neuropathology, the first being held in Rome in 1955. It seems appropriate to mention that there were already more than 800 attendees at the 4th congress, in München in 1961, among whom 142 Americans, 92 Germans and 42 from England. In the USA, neuropathology became an independent discipline in 1959.

The British Neuropathology Society was the second to be established, in 1950. There were five full-time neuropathologists in the preparatory period of 1945-1950; by 1962 there were 32 full-timers, on the basis of a detailed training programme over a span of 6 to 8 years. Neuropathology in England is a separate specialty. The training period closes with a written and oral examination by the College of Pathologists.

In the Netherlands, the twelve colleagues in part-time or full-time neuropathology, together formed a recognised 'Section of Neuropathology' within the 'Netherlands Society of Psychiatry and Neurology', on February 28th, 1953. The Section held several meetings over a period of three to four decades with representatives of the 'Association for Pathological Anatomy' to work out a sound training curriculum. In 1966, the Section modified its statutes and bore the name 'Netherlands Society for Neuropathology'. A second notary-endorsed change of statutes was necessary in 1985; training criteria were nearly agreed upon with the Association of Pathology in 1992.

The Japanese followed soon after: they founded their Society of Neuropathology in 1959 with 40 full-timers. Almost immediately, neuropathology was officially recognised as a specialty in its own right. The Japanese also founded their own journal, *Neuropathology*. In the nineties, the society counted about 150 members.

In 1965, thanks to initiatives of the English and of the World Federation of Neurology (WFN), the 'International Society of Neuropathology' (ISN) was established. It was ratified at a meeting in Copenhagen in 1967. However, the full constitution and bye-laws of this body had already received unanimous support from the WFN. The WFN founded the official journal, the *Acta Neuropathologica*, in 1961 with F. Seitelberger as editor-in-chief. Dr. Marion C. Smith of the National Hospital, Queen Square, proved to be a most active and meticulous ISN-secretary; her bi-annual ISN-Newsletters were as informative about the organisational history of neuropathology as they are a delight to read. The members grew to number 850. The International Society of Neuropathology founded the journal *Brain Pathology* in 1990. In 1975, the British neuropathologists founded their own journal *Neuropathology and Applied Neurobiology*.

In the meantime, neuropathological societies had been founded in Austria, in Germany – where neuropathologists and neuroanatomists justifiably and quite shrewdly joined rank in 1955 ('Deutsche Verein für Neuropathologie und Neuroanatomie', a name changed to 'Deutsche Gesellschaft für Neuropathologie und Neuroanatomie' in 1976), East-Germany 1969, Italy 1973, Poland 1973, Canada 1973, Ireland 1973, Switzerland 1964, Australia and New Zealand 1970, to name a few.

The West Germans succeeded in obtaining the governmental creation of two Chairs of Neuropathology in Giessen and in Marburg. In Germany, neuropathology was recognised in 1987 by the national medical board as an autonomous discipline and provides a six year training (two years pathology, three years neuropathology and one year clinical neurology). In Poland, too, it is an independent specialty.

A 'European Society of Neuropathology' was established in the 1980s, leading to a charter for fifteen countries and fixing a training programme; it was agreed upon by the Union Européen Médicins Spécialistes (UEMS), which recognises 27 specialties. Seven European and 14 International Congresses of Neuropathology have already been held. In 1981, a fifth journal appeared on the market: *Clinical Neuropathology*, testifying to the mondial emancipation of the specialty.

During the second half of the twentieth century most Dutch neurological university departments disposed of a neuropathologist and his laboratory within the departmental confines (VU and Municipal University Amsterdam, Leiden, Utrecht, Nijmegen). The official training programmes for neurological residents included obligatory attendance at brain-cutting sessions (at which the resident read out the case history of the deceased and the radiologist showed pertinent radiograms), monthly neuroclinical-pathological conferences, and two to four months of full-time courses in the neuropathological lab, during which the residents had standard sets of slides of typical basic elements and features of neurological disease at their disposal, received pertinent tuition, and were supervised by the neuropathologist. Over the recent decades this type of curriculum has gradually gone into disuse through neglect.

A detailed analysis of the factors at play that have led to the ultimate failure of the Dutch Societies of Pathology and of Neurology (the latter supported by those of Neurosurgery and of Psychiatry) to agree on a mutually and officially endorsed training programme for neuropathologists would exceed the space allotted for this chapter. In retrospect, the minutes of the numerous meetings of representatives of these societies over a span of 40 years form the dialogue of a tragi-comedy soon to be ended by the fall of the final curtain. The chance to create a harmonious solution of differences in opinion (such as occurred in Germany, Poland, England, Japan, USA, etc.) and to open up an autonomous discipline has been missed. The Dutch can boast of the dubious distinction of being (with Belgium) one of the few Western countries in which a governmentally recognised specialty of neuropathology remains utopia instead of reality.

Today, routine autopsies are refused with increasing frequency by the families of deceased patients. The ever-growing use of various NMR-modes throughout the country's hospitals make post-mortem verification quasi-redundant in many instances. Over the last decade, the terror of economising on healthcare has resulted in the progressive disappearance of centres where neuropathology is carried out and can be taught. A deficiency in good will, of mutual trust, combined with a surplus of short-sighted and narrow-minded obstinacy and impotence of the parties involved or to be involved (specialist societies, specialist registration body, boards of hospitals and of medical faculties, the semi-governmental 'Central College') joined forces to breed the actual miserable state of affairs.

The present writers, *bien nourri dans le sérail*, would be willing to carry out an autopsy of the process, if it was felt that such an exposé would help to provide crucial clues for a solution. For the moment, however, this chapter must conclude with the observation that the history of neuropathology in our country ends on a lamentable note. Although this is sad, there is some hope because (experimental) neuropathology has a great future, in view of the vast field of exploitation of the growing number of known mutated gene-products (proteonomics), in analysing the effects of these gene-products on neural cells. Given such (immunochemical) tools, it already enjoys an ever-greater potential to clarify psychiatric disease and could now well be applied to close the optimistic, idealistic circle which started 150 years ago in Germany: Geisteskrankheiten sind Gehirnkrankheiten [Mental diseases are brain diseases].

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Neuroradiology 10

J. Valk and J.T. Wilmink

The discovery by Wilhelm Conrad Röntgen of "Eine neue Art von Strahlen" [a new kind of rays, then named X-rays] in 1895 had a great impact on the development of modern physics, and revolutionised medical practice. Recognition of the importance of this discovery was global and instantaneous.

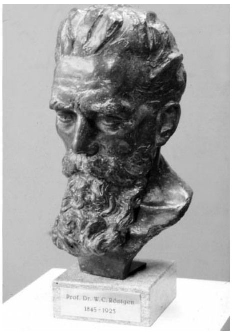

Figure 1. Wilhelm Conrad Röntgen. First winner of the Nobel prize for physics.

Introduction of X-ray diagnosis and therapy followed within one year, and in the Netherlands must probably be attributed to the pediatrician Van Wely, founder of the Children's Hospital in The Hague, who reported about the first results of X-ray diagnosis at the IXth meeting of the Pediatric Society (1896). The work of J.K.A. Wertheim Salomonson (see also Chapter 29), who was also the first to publish work on X-rays in the *Dutch Journal of Medicine* in 1896, was of decisive significance. He played a major role in the improvement of X-ray tubes, eventually leading to an important Dutch X-ray industry. He was also the first professor of Radiology and Neurology in the Netherlands and founder of the Dutch Society of Radiology.

The stages of development of neuroradiology in the Netherlands

Chronologically, with some overlap, we can recognise at least three stages in the development of neuroradiology in the Netherlands, each characterised by a certain stage of technical development:

The early stage, 1900 - 1920, in which plain X-ray photography played a major role, and in which especially skull-radiology and oto-radiology flourished. In this period, the Viennese school, with names such as of A. Schüller and E.D. Mayer (both eponyms for their respective projections of the petrous bone), was famous and visited by students and radiologists of many nationalities.

The search for new projections that would shed light on special parts of the skull led to the description of a number of techniques, which were applied on a large scale in radiological departments. Among them are many projections of the petrous bone, Pöschl, Guillain (views of the ossicles in the cavum tympani), balayage of Chaussée (incremental stereoscopic views of the contents of the petrous bone), Stenvers projec-

Figure 2.
Skull X-rays appear empty unless calcifications are present as in this Maroccan boy with a parasitic infection.

tion (inner auditory canal, longitudinal view of the petrous bone), and projections of the sphenoid bone and the optic foramen, of which those developed by Rheese and Stenvers were the most popular. (See for details on these projections: Zonneveld 1987.)

The second stage, 1918 – 1970, is the period of the development of differentiation methods in radiology. Two discoveries were particularly important in this period and had a major impact on neuroradiological practice.

The first was the use of contrast media, starting with the use of air as negative contrast medium in ventriculography and encephalography by the neurosurgeon W.E. Dandy, followed by the use of positive water-soluble contrast agents, used for intravenous applications and later also for cerebral angiography (Edgar Moniz 1927), and lipid-containing contrast media for myelography (J.A. Sicard and Forestier 1921). Some of these contrast media had postponed side effects with occasional life threatening consequences. Lipiodol and pantopaque caused a severe adhesive arachnoiditis (even years after injection), while thorotrast – used for direct percutaneous carotid angiography – caused thorotrastomas in the liver, or, when injected subcutaneously during the angiographic procedure, in the neck. Later in the century, water soluble contrast media, first ionic, later non-ionic, were developed, with considerable diminution of acute and long-term side effects. The introduction of a water-soluble contrast medium for intrathecal use improved the quality of ventriculography and myelography.

This was also the period in which neurosurgeons and neurologists performed their own neuroradiological examinations. Both technical developments and time constraints were probably responsible for the gradual shift of the execution of these procedures to full-time neuroradiologists. The contributions of the neurosurgeons T.A. Lie and H. Verbiest, on congenital anomalies of the cranial vessels and congenital and developmental narrowing of the spinal canal plus examinations of the posterior fossa respectively, gained worldwide recognition.

The second discovery was the development of radiological differentiation methods, which reformed neuroradiology such as pluridirectional tomography and subtraction angiography (as well as 'autotomography'), both invented by Bernard George Ziedses des Plantes (another neurologist and radiologist) and described in his thesis in 1934. These methods had in common that they eliminated the superimposition of other structures on the structures of interest. Pluridirectional tomography became widely used in radiology, soon after its description in 1934. It greatly improved the images of the orbits, the sphenoid, the petrous bone and, in particular, the middle and inner ear, where incredible submillimeter resolution showed the chain of ossicles, the cavum and tegmen tympani, the round and oval windows, the canalis facialis, the cochlear windings, vestibulum and labyrinth. The method was also used in combination with negative (air) contrast studies, such as pneumo-encephalography and pneumo-myelography.

Figure 3.
Holder for suboccipital puncture for pneumencephalography as developed by Ziedses des Plantes.

It took much longer, in fact 35 years, before subtraction angiography became an integral part of routine neuroradiological practice. In the digital period, electronic instant subtraction became the hallmark of digital subtraction angiography.

The third stage, 1970-2000, is the period during which computers were introduced in the imaging process together with the principle of axial tomography. The elements for computerised axial tomography were all present in the sixties. Scintillation crystals were known to become proportionally fluorescent when hit by an X-ray beam, electronic engineering was developed sufficiently, and computers, though big and clumsy, were available. The only thing needed was someone with the vision to bring the components together and with sufficient fantasy to realise that films were not absolutely necessary as primary substrate for image display. This man was Nobel laureate, Godfrey Newbold Hounsfield. The main advantage of these computer-assisted modalities was initially the much higher contrast resolution that could be achieved by digital handling of the acquired data. Conventional, analogous, X-ray methods only differentiated structures with great difference in density, such as bone and air. Therefore, the skull appeared to be empty on plain X-rays and conventional tomography. Godfrey Hounsfield worked in the research laboratories of EMI. This company also owned the record company His Master's Voice, which had the Beatles under contract (after they had been turned down by DECCA record company!). Thanks to the money available to this firm, Godfrey Hounsfield was able to continue his research on pattern recognition and the development of computer-assisted imaging processes. From the original concept it took many years to develop a machine that could be used in clinical practice. The first prototype was placed in the Atkinson Morley Hospital. On the very first X-ray CT scanner the brain itself became visible. This, again, was a major leap forward. Management of acute neurological patients changed radically, and the quality of diagnosis of spinal abnormalities increased considerably.

The first CT scanners in the Netherlands were placed in the Ursula clinic in Wassenaar and the Wilhelmina Gasthuis (later the Amsterdam Medical Centre) in 1974. Because of restrictive governmental policy the number of CT scans installed in the Netherlands increased only slowly.

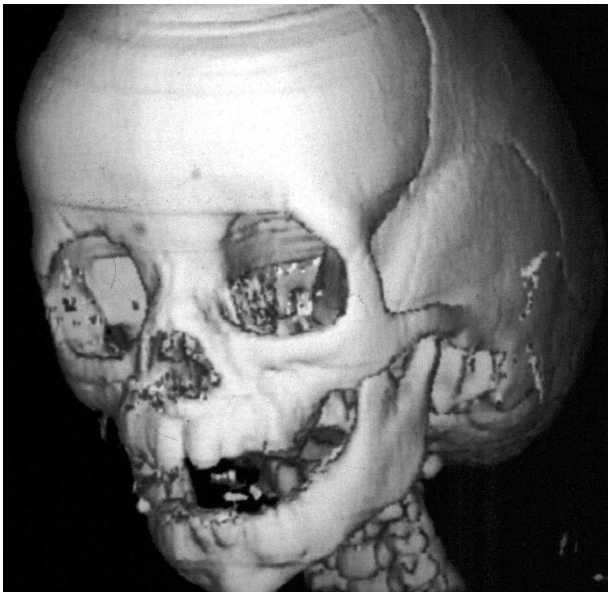

Figure 4.
CT proved to be very important in emergent neurological problems. Although partially replaced by MR there are still important indications for CT. One is illustrated here in a 3D reconstruction of a dysplastic skull. These images are essential for planning reconstructive surgery.

The first CT scanners were head scanners. The patient's head was enveloped within a waterbag and the 'gantry' (X-ray tube and detectors) rotated around the head with increments of a few degrees. The resolution was initially poor (84x84, later 128x128) and acquisition times were very long. Despite these shortcomings CT revolutionised neurological practice. CT, MMnow as whole body scanner, found its niche first in emergency rooms. It showed its value especially in the diagnosis of acute haemorrhages, cerebral contusions, subacute infarctions, maxillo-facial, temporal bone, orbital and spinal fractures. In (sub-)chronic conditions, CT proved to be extremely helpful in the diagnosis of congenital anomalies of the skull, brain and spine. Multiplanar and 3D reconstructions refined these diagnostic possibilities. By the end of the 20th century, CT had developed into a fast and reliable imaging modality with high-resolution power. The sub-millimeter resolution also made CT valuable in the diagnosis of head and neck radiology. The work of F.W. Zonneveld (1987)on CT of the temporal bone and orbit deserves special mention (CT, for the foreseeable future, will maintain its role for a number of neurological indications. However, it does have a number of disadvantages. CT uses ionising radiation with the well-known risks, and, because of the single parameter 'X-ray absorption' used for the formation of images, density resolution is limited. For example, lesions of a common disease such as multiple sclerosis can be hardly seen or not at all be seen on CT. Beam-hardening artifacts can make a diagnosis in the posterior and lower middle fossa difficult.

At the end of the 1970s, a new modality, Magnetic Resonance Imaging, emerged with a solution to most of the problems that could not be solved by CT.

The 'free induction decay', the MR signal was simultaneously discovered by Bloch and Purcell (1945). Magnetic Resonance is based upon the absorption and subsequent release of energy of radio-frequent pulses with a specific frequency by protons, brought into a resonant condition by a strong static magnetic field. To locate the weak signal response of the protons in human tissue, Damadian (1971) and Lauterbur (1973) developed methods to locate the signal in space. The first clinical system was developed in Nottingham in 1974 by Hinshaw and Moore, and much of the fundamental work in adapting the method to clinical practice was done by Peter Mansfield (later Sir Peter Mansfield), who developed at the start the echo-planar sequence, now the cornerstone of functional MRI.

Magnetic Resonance Imaging (MRI) started in the Netherlands with a prototype

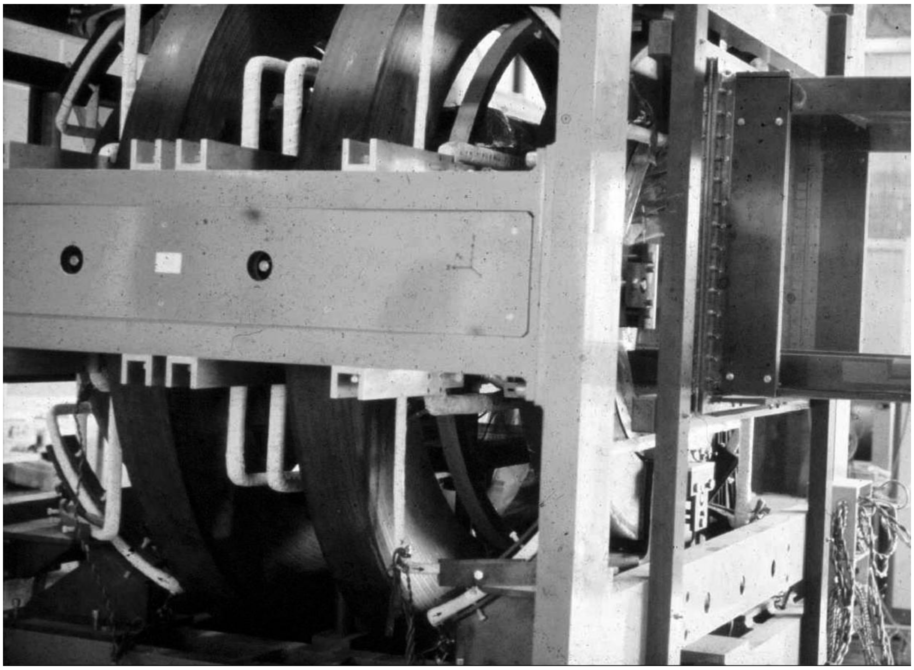

Figure 5.
The first prototype MR scanner in the Netherlands in the factory of Philips in Best. It was an open electromagnet with water cooling and with the Faraday cage around the patient.

machine in the Philips' factory in Best, under supervision of André Luiten and with clinical input from two radiotherapists (Vermey and van Peperzeel) and two radiologists (Van Voorthuizen and Valk). This was a water-cooled electromagnet with a field strength of 0.15 Tesla. Despite the initially long scanning times and low spatial resolution it became clear to those who worked with the prototype that the sensitivity of MRI with regard to brain lesions was many times higher than of CT. The first book describing this technique appeared in the Netherlands in 1984 in both a Dutch and an English version (Valk, MacLean and Algra).

The first clinical system was installed in the University Hospital Leiden (0.15 T Philips) in 1983 and the second one in the Vrije Universiteit Hospital in Amsterdam (0.6 T Technicare) in 1984. It took another ten years before MRI imaging was introduced nationwide. MR has several advantages over CT. In addition to the absence of ionising radiation, the image formation is based upon a great variety of both machine and tissue parameters.

Machine parameters can be used in such a way that the maximum information is extracted from the examined tissues. Another very important feature of MR is the possibility to choose freely any imaging plane without moving the patient. The sensitivity of MR to detect pathological tissue proved to be many times greater than that of CT. The first example of that sensitivity was the detection of multiple sclerosis lesions in the brain (Young and Bydder, Lancet, 1983), which had been only sporadically possible with CT. A second great breakthrough was the visualisation of the progress of myelination in neonates and infants, not visible on CT. Over the years, the specificity of MRI findings also increased. Furthermore, MR can be used to collect physiological data, for example, by diffusion-weighted and perfusion imaging, and to obtain biochemical data by applying MR spectroscopy. In addition, functional MRI allows one to visualise brain activation by different stimulation tasks,

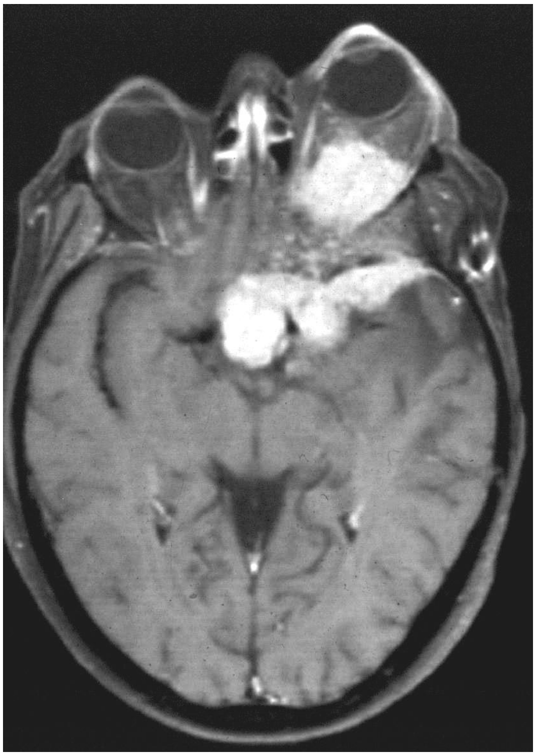

Figure 6.
MR makes it possible to highlight pathological processes and to suppress normal tissue as shown here in a T1-weighted, fat-suppressed, gadolineum-enhanced image.

simple or complex. The latter made the entry of MRI in neuropsychological and psychiatric research possible. These capabilities have made MR contributions unique and have made MR the instrument of choice in neurological and neurosurgical diagnosis and research of brain functions and brain physiology.

Interventional neuroradiology (starting in the 1950s)

Radiology in general is no longer solely a diagnostic specialism. More and more radiologists are involved in therapeutic procedures. This is also the case in neuroradiology. In the early days, percutaneous embolisation was initiated in pathological processes with vascular supply via the external carotid artery, such as glomus tumors (Hekster 1976), angiofibroma's and traumatic and non-traumatic epistaxis (Valk 1984).

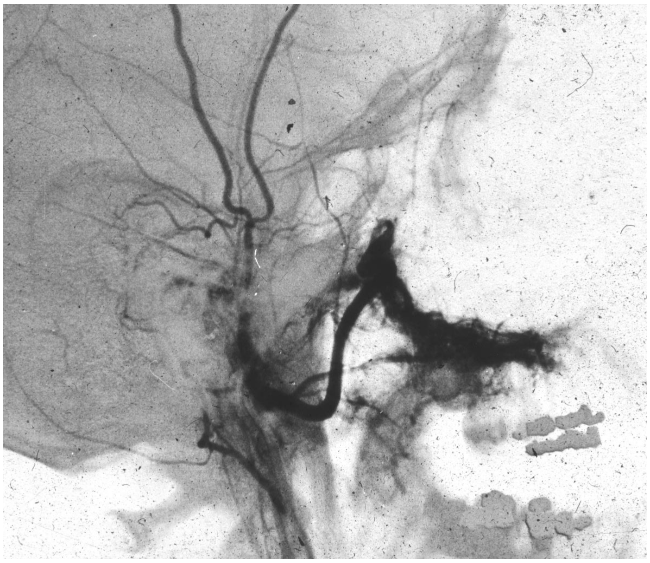

Figure 7. The first endovascular interventions were done in the external carotid territory, as demonstrated here in a 17 year old girl with a hemangioma of the right maxilla as part of a Wyburn-Mason syndrome.

Later, detachable balloon techniques were used in the obliteration of carotido-cavernous fistulae and, in the last decade of the century, with the development of detachable coils (Guglielmi-coils), the endovascular occlusion of intracranial aneurysms and the selective embolisation of arterio-venous malformations became an accepted way of treating vascular malformations (F. Peeters, W. van Rooy, M. Sluzewski).

The role of radiology in this field is growing rapidly. In stroke units, intra-arterial fibrinolysis demands the placing of microcatheters in the obstructing clot. With caution and careful selection of patients, percutaneous angioplasty, with or without stenting of carotid arteries has become an option, as has angioplasty of intracranial vessels. Further refinement of these techniques will follow in the present century.

Figure 8.
Endovascular treatment of aneurysms has become an option. In this patient, a large top-of-the-basilar aneurysm has already been coiled; a second aneurysm of the carotid syphon is under attack.

Shapers of neuroradiology in the Netherlands

J.K.A. WERTHEIM SALOMONSON (1864-1922)

Wertheim Salomonson (see also Chapter 29) realised immediately the significance of Röntgen's discovery for medical purposes. He also realised that the technique needed improvement and prompted a glassblower in Amsterdam to make a better X-ray tube. The first Dutch X-ray tube was produced in 1896. It was the basis for an important Dutch X-ray industry. In 1899 Wertheim Salomonson was appointed professor of Neurology and Roentgenology. He was one of the founders of the Dutch Society of Electrotherapy and Roentgenology in 1901. The gold medal for scientific work of the Dutch Society of Radiology bears his name.

H.W. STENVERS (1889-1973)

Stenvers (see also Chapter 26) was a neurologist, who dedicated only some of his time to radiology. In both areas of interest he became well known for his careful and precise approach both in clinical and scientific work. As a clinical neurologist he was appointed head of the X-ray department of the University of Utrecht. This department at the time consisted of one room with a primitive X-ray installation. During the First World War he combined military service with scientific work, mostly studies of X-rays of the skull and various projections. In 1916, a publication of his in the *Dutch Journal of Medicine* dealt with X-ray diagnosis of processes in and around the orbit. In 1917, he published an article in the same journal concerning 'X-ray photography of the petrous bone'. He developed a projection that showed the apex of the petrous bone, the porus and meatus acusticus interna, the cochlea, labyrinth, mastoid cells and the temporomandibular joint.

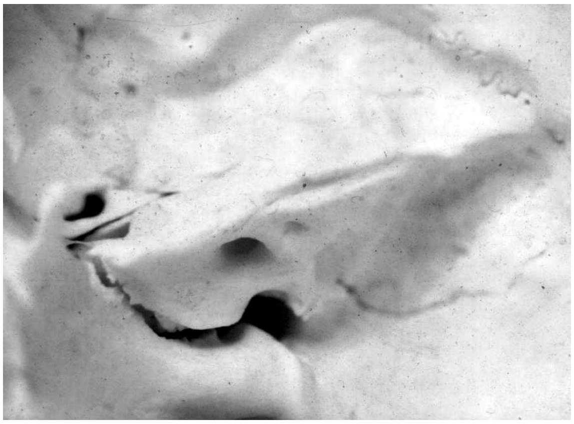

Figure 9.
The Stenvers view of the petrous bone was achieved by two 45 degree angulations of the central beam vs the orbitomeatal plane, resulting in a longitudinal view of the petrous bone.

This projection was named after him: the Stenvers projection. In the following years he exploited this technique by showing the impact on the petrous bone of a wide variety of pathological conditions. His most important contribution to radiology was a standard text that appeared in 1928: *Röntgenologie des Felsenbeines und des bitemporalen Schädelbildes* [Roentgenology of the petrous bone and of the bi-temporal skull].

G.J. VAN DER PLAATS (1903–1995)

Van der Plaats (GJ) played a very important role in the development of radiology and, consequently, of neuroradiology in the Netherlands. He practised radiology from 1928-1968, first in Utrecht, followed by Eindhoven and Maastricht, the latter combined with a three-year period as part-time professor in Groningen, from 1955-1958. His fundamental work included stereoscopy, gamma ray techniques, dose estimation and dose reduction, and magnification techniques with X-ray tubes of small focus, image-intensifier technology, and cinematography. With the aid of these techniques he improved radiological practice in general, but in addition made special stereoscopic examinations of the skull and the spine. He became internationally known as the instigator of training for residents and technicians, and his basic work was translated into many languages: *Medische Röntgentechniek* (1953 [Medical Roentgen Techniques]). For a long time this work was the basic text used by both residents in radiology and technicians.

L. PENNING (1924–)

When appointed in Groningen, Van der Plaats took Lourens Penning with him to ensure continuity. Penning was eventually appointed radiologist in the staff of the department of neurosurgery under the neurosurgeons Lenshoek and, later, Beks. He was the first radiologist to become involved in neuroradiology on a full-time basis. He was greatly interested in the dynamic aspects of animal and human anatomy and his thesis in 1960 dealt with functional pathology of the cervical spine. This work was beautifully illustrated by drawings from his own hand. In collaboration with the neurosurgeon Braakman he wrote a classic textbook: *Injuries of the Cervical Spine*. In his later work Penning also included the lumbar spine, a field in which he is still active. The hallmark of his work is the meticulous analysis of the normal anatomy and the description of the movements of the spine.

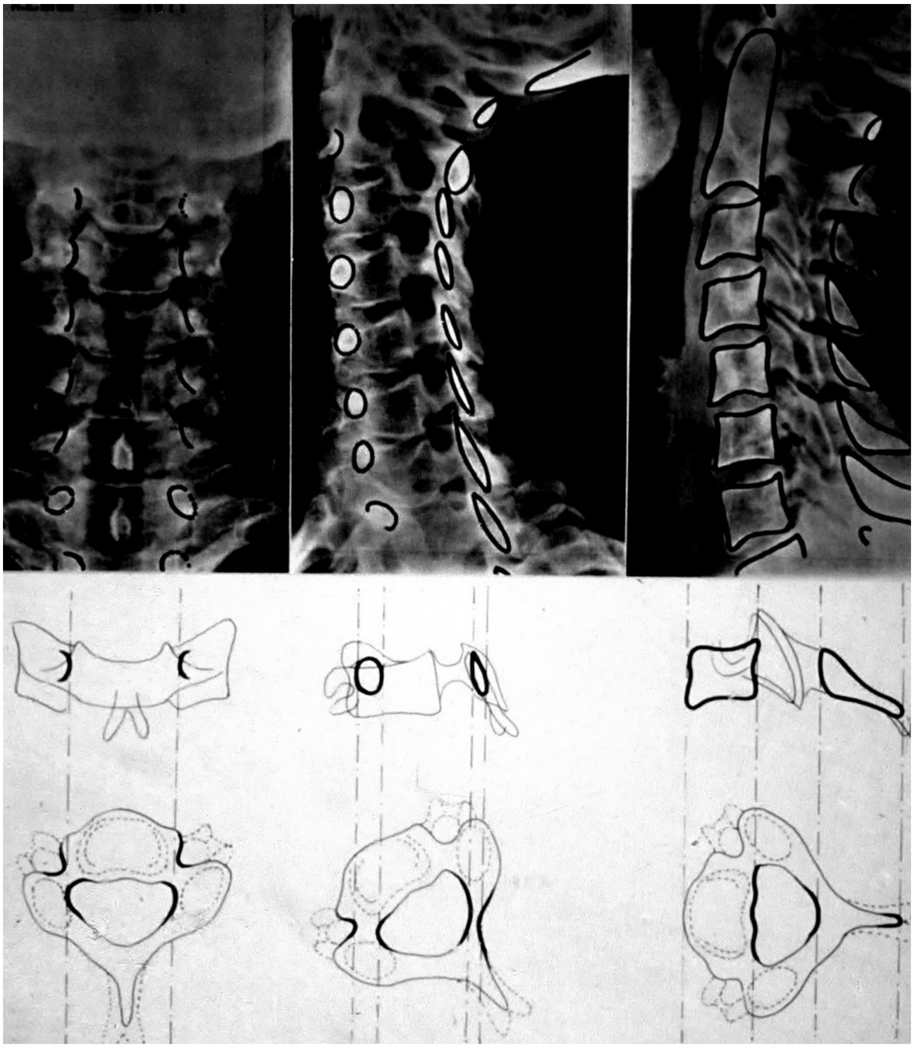

Figure 10.
Example of the drawings as made by Penning to analyse structure and function of the cervical spine.

Lourens Penning was appointed lector in Neuroradiology in 1964 and full professor in 1970, the first chair of Neuroradiology in the Netherlands. Penning did important work on brain scintigraphy resulting in a major work together with Front, in 1975, dealing with the new technique of dynamic serial scintigraphy.

CT studies were added to his research, aided by Wilmink, who also added the information obtained by Magnetic Resonance imaging to the studies of the spine. When, after Penning's retirement, the chair of Neuroradiology was discontinued in Groningen, Wilmink was appointed professor of Neuroradiology in Maastricht where he continued his studies on the spine.

Figure 11.
Lourens Penning.

B.G. ZIEDSES DES PLANTES (1902-1993)

A small man , over 80 years of age, bald, with heavily rimmed glasses, runs through the streets of his neighbourhood holding a child's windmill, frowned upon by the neighbours, he concentrates on the blades of the propeller to test a new idea on a more energy saving, fully-feathering propeller. The name of this remarkable person: Bernard George Ziedses des Plantes, professor of Radiology, inventor for life, the internationally renowned neuroradiologist, from whom was withheld the practice of neuroradiology in his own University Hospital, the Wilhelmina Gasthuis in Amsterdam. Fortunately, he was welcomed at the Valerius Clinic, then the categorical neuropsychiatric dependance of the Academic Hos-

Figure 12.
B.G. Ziedses des Plantes after his retirement.

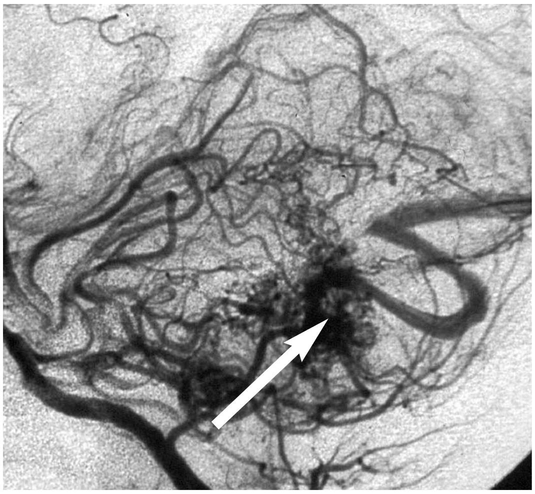

Figure 13.
Digital subtraction angiography has become the standard technique in conventional angiography. This image shows an arteriovenous malformation in the posterior fossa.

pital of the Vrije Universiteit. Those who have worked with 'the little professor from Holland' know that his way of looking at things, which are considered commonplace or taken for granted by others, is with an inquiring interest as if he is seeing something completely new. An incidental question could provoke a long silence and a three-month wait before a completely unexpected, thoroughly worked-out response was given. Every new clinical case became a new challenge.

He had a striking talent to see through a problem, reducing it to simpler, solvable dimensions. Elastic bands and bits of meccano formed the major tools in the development of new constructions. For the X-ray department, the inventions of Ziedses des Plantes ranged from a simple headholder for pneumoencephalography and a manually operated stereotactic apparatus for lamina terminalis perforation in hydrocephalus, to a self-developed instrument for multidirectional tomography of such craftsmanship that it still performed perfectly after more than forty years, and could compete with modern factory-made equipment.

In his thesis (1934), Ziedses des Plantes described – in his usual detailed way – planigraphy (later named tomography by the International Commission on Radiological Units and Measurements) and subtraction. Tomography found its niche in radiology right away. It took, however, nearly thirty years before the significance of subtraction angiography was recognised worldwide. Other inventions, such as serioscopy, never made it into clinical practice.

In his clinical work, Ziedses des Plantes showed the same ingenuity. He was the first to publish on direct and indirect autoradiography (scintigraphy) and one of the first to describe (1950) the consequences of lumbar disc herniation. He conceived the so-called somersaults in pneumoencephalography with small quantities of air (1950). Not one of his scientific publications contained anything but his own inventions and his own concepts.

He received worldwide recognition for his work and was appointed president of the International Symposium of Neuroradiology in 1949. Among the many trophees he received figure the Schleussner Röntgenpreis (1934), the Reinier de Graaff medal (1970), the Gold Medal of the International Congress of Radiology (1973), and the Gold Medal of the European Congress of Radiology (1991). The 'German Society for Neuroradiology named their award after him. He was an honorary member of many national societies: the Italian, Australian, German, American, and, of course, the Dutch Society of Radiology. His former students edited a book, *Selected Works of B.G. Ziedses des Plantes*, on the occasion of his 70th birthday, which was edited by Excerpta Media in 1973, and in which his most important works are brought together.

J. VALK (1929–)

Figure 14.
J. Valk.

Valk first trained as a neurologist-psychiatrist and practiced as such for seven years. During his training he worked for several years under the guidance of Ziedses des Plantes. He continued to perform neuroradiological examinations of neurological and psychiatric patients and his thesis was a neuroradiological study of chronic psychiatric patients (1971). His promotor was Ziedses des Plantes. When he decided to become a full-time neuroradiologist, Ziedses des Plantes asked him to train with him and become his successor at the Valerius Clinic. Neuroradiology moved with Neurology and Neurosurgery from the Valerius Clinic to the Academic Hospital, Vrije Universiteit and Valk was appointed professor of Neuroradiology (1978) and, in 1981, professor of Radiology and head of the department of Radiology (1981). He succeeded in acquiring one of the first Magnetic Resonance systems in the Netherlands for the Vrije Universiteit. In 1984 he published a book on the *Basic principles of Magnetic Resonance Imaging*, in 1987 *MRI of Brain and Spine, a Teaching Atlas*, and, in a very fortunate combination with child neurologist prof. Marjo van der Knaap, developed a computer-assisted pattern recognition programme for white matter disorders in children, that received international recognition. They wrote many articles together on white matter disorders in children culminating in a standard text: *Magnetic Reso-*

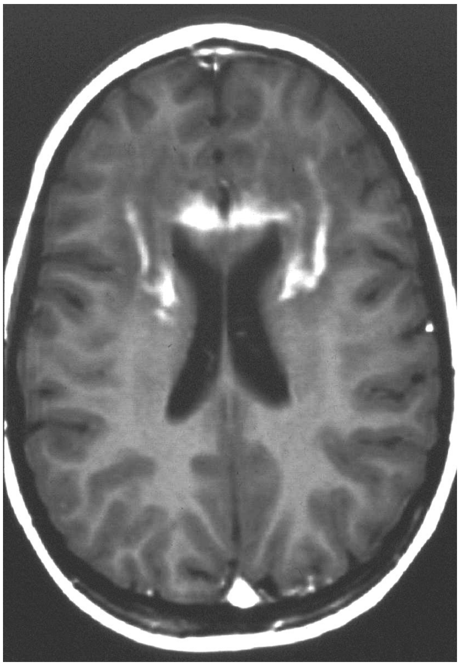

Figure 15.
10 year old boy with X-linked adrenoleukodystrophy, with bilateral symmetric involvement of the frontal white matter. This unusual frontal, in stead of occipital, location occurs in about 10% of cases. These data were obtained by the pattern recognition program of M.S. van der Knaap and J.Valk.

nance of Myelin, Myelination and Myelin Disorders (1991, second edition 1995). The pattern recognition programme also led to the description of several hitherto unclassified white matter disorders, work that is still being continued today, with expansion into biochemical and genetic research. For this work they received the Gold Award of the International Society of Magnetic Resonance in Medicine.

Together with Professor O.E. Hommes, Valk laid the basis for an MR centre dedicated to the study of Multiple Sclerosis. With the help of the 'Foundation Friends of MS research', this centre has been established at the Vrije Universiteit, Amsterdam, and has shown its scientific merits over the past five years under the leadership of Chris Polman and Frederik Barkhof.

Valk is an honorary member of the Dutch Society of Radiology, the Dutch Society of Neuroradiology, the Royal Belgian Society of Radiology, and the Turkish Society of Neuroradiology. For his scientific work he was awarded the Cornelia de Lange medal of the Dutch Society of Child Neurology, the Wertheim Salomonson medal of the Dutch Society of Radiology, and the Gold Medal of the International Society of Magnetic Resonance in Medicine.

Valk, in cooperation with Wilmink, succeeded in making the Dutch Society of Neuroradiology the first recognised sub-specialty section of the Dutch Society of Radiology. In 1985, Valk hosted the Congress of the European Society of Neuroradiology, in 1995 the Basic Course of the ESNR on the Skull Base (with Jan Wilmink), and in 1998 the European Society of Magnetic Resonance in Neuropediatrics.

The Dutch Society of Neuroradiology

The Dutch Society of Neuroradiology (DSNR) started as an informal meeting of neuroradiologists on the initiative of George Ziedses des Plantes and Lourens Penning in the 1950s. It took many years of near-death and resuscitations before these meetings became more structured. Lourens Penning as chairman of what could then be considered a working-group installed the rules of the society, further implemented when Jaap Valk took over the chair. There was now a formal board with a secretary and a treasurer. Valk and the vice-chairman, Jan Wilmink, opened the discussions with the Dutch Society of Radiology, to become officially recognised as sub-section of this society. They succeeded in obtaining this status and the right to use the name 'Dutch Society of Neuroradiology' in 1992. The way was now free to present this society with a programme of its own and with bi-annual conference courses on specific topics, which proved to be very successful The chair was taken over by Jan Wilmink in 1996 and by Paul Algra in 1999. International contacts with the European Society of Neuroradiology were established as well as with the World Federation of Neuroradiological Societies.

Concluding remarks

Magnetic Resonance Imaging, MR Spectroscopy and MR Neurofunctional Imaging have opened up new areas of research in neurosciences. It is clear that neurologists, neuropsychologists and neuroscientists welcome the possibility to extend their in vivo research. Because no ionising radiation is involved, (neuro-)radiologists cannot claim the exclusive right to operate these tools. To survive, neuroradiologists should become partners in a team of researchers, where their added value may lie in better knowledge of MR anatomy as brought about by different MR sequences, better knowledge of MR possibilities, insight in neuronal circuits and understanding of pathophysiological processes and changes induced by stationary or progressive disease as reflected in MR. In other areas, such as routine diagnostic and follow-up studies, there will be a role for neuroradiological expertise.

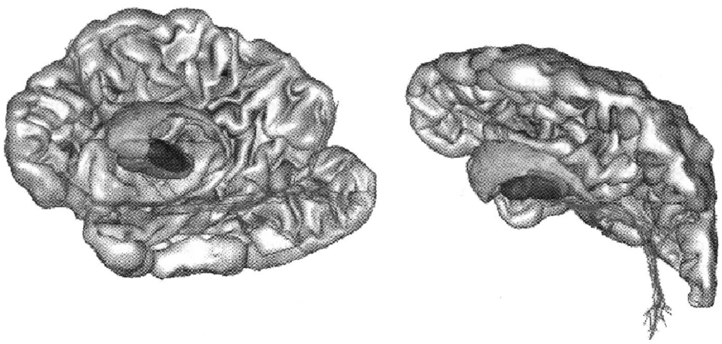

Figure 16. Modern MR techniques, such as diffusion tensor mapping allow fibre-tracking of the white matter tracts. One of the many new possibilities in MR Figure from the godfather of diffusion weighted imaging (Denis le Bihan).

In interventional neuroradiology there will certainly be a place for devoted neuroradiologists, even if this area is partly shared with other disciplines. In a European context, attempts have been made to define the contents of a training programme for neuroradiologists. So far, this has not resulted in recognition of neuroradiology as a super (sub-)specialty and it is questionable whether it ever will. In the Netherlands, the number of chairs for neuroradiology at academic hospitals does not reflect the importance of the subspecialty. Only three of the eight universities in the Netherlands hold such a chair at the moment.

Today, many neuroradiological examinations in the Netherlands are performed and interpreted by radiologists who have no training in neuroradiology, and who had at best some exposure to neuroradiology during their residency. This means that the reports of neuroradiological studies are mainly descriptive and superficial. This is a worrying trend and may lead to a situation where other disciplines will move in to fill the gap that is now widening between technical-anatomical competence and clinical expertise and interpretation.

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Clinical Neurophysiology 11

E.J. Jonkman

It is impossible to write the history of clinical neurophysiology in the Netherlands as a continuous story: World War II caused such a break that it is necessary to describe the events before and after 1945 in two separate sections. Moreover, as will be described in the first section, clinical neurophysiology before the war was almost completely confined to electroencephalography, while in the years after the war many other techniques became available, which will be mentioned successively in the second section. The third section contains a short history of the Dutch Society for Clinical Neurophysiology and the international activities of the Society and its members. The fourth section gives some information on the activity of Dutch neurophysiologists in writing doctoral theses and publishing in international journals. A survey of training facilities for neurophysiologists in the Netherlands is given in section 5.

1 The period between 1936 and 1945

Although the existence of cortical electrical activity in animals had already been demonstrated in the nineteenth century, it took until July 6th 1924 before Hans Berger succeeded in recording an electroencephalogram (EEG) in a patient with a brain tumour. He then waited five years before publishing his results (Berger 1929). His observations remained unrecognised until the spectacular demonstration of an EEG recording by Adrian and Matthews for the British Physiological Society on May 12, 1934 (Adrian 1971).

At that time there was already a considerable interest in the EEG in the Netherlands. In 1936 the physicist Koopman described a cheap method to convert an electrocardiograph (Fig. 1) into an electroencephalograph by adding a simple pre-amplifier (Koopman and Hoelandt 1936). In the same year L.J. Franke, a neurologist/psychiatrist, published a booklet in which he presents his first clinical EEG results (Franke 1936). After confirming the results of Berger (Fig. 2), Franke added new EEG observations, for example, on the influence of hypoglycaemia on the EEG. A first approach to EEG monitoring is also mentioned in this first Dutch publication: the EEG is considered useful to measure the sleep level in psychiatric patients who are treated with prolonged sleep.

Although their apparatus was rather primitive, Franke and Koopman were well aware of the specifications needed for a good recording. The necessity for EEG machines to have a good linearity and ample frequency characteristics, and the problems arising from phase-shifting are already mentioned in one of their next publications. There was even an attempt at manual (!) Fourier analysis of EEG waves (Franke and Koopman 1938).

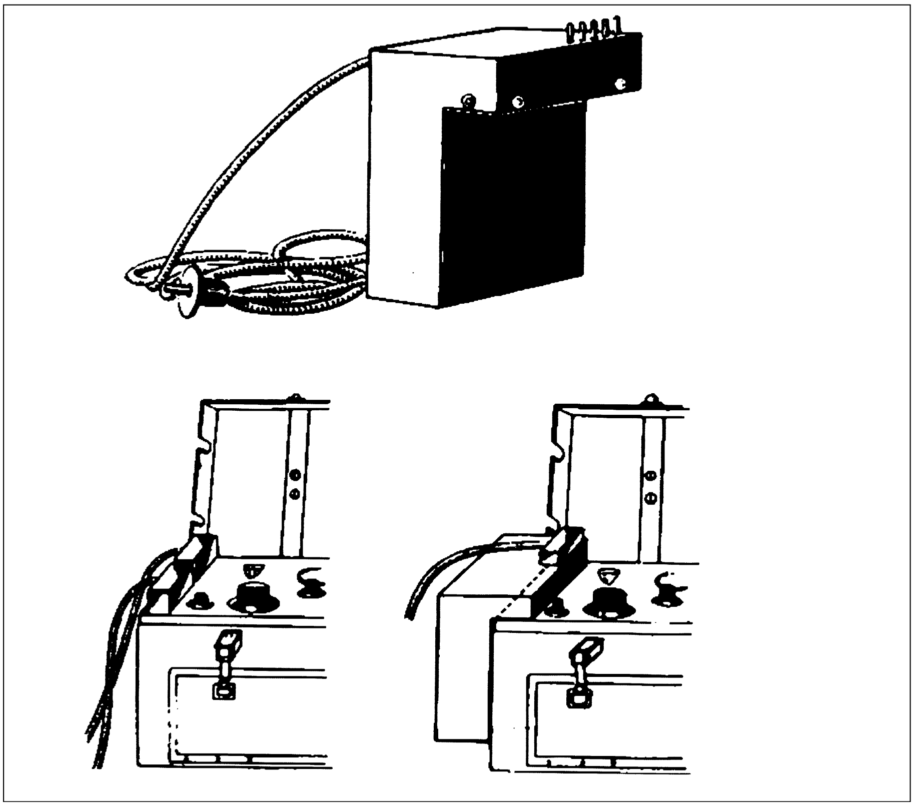

Figure 1.
The first EEG machine built in the Netherlands around 1935. A pre-amplifier is added to a commercially available – battery driven – Siemens cardiograph.

In the 1930s the origin of the transcranially recorded cortical rhythms was uncertain. Berger more or less regarded the alpha-rhythm as a phenomenon produced by the brain as a whole, whereas Adrian (Adrian and Matthews 1934) pointed to the occipital lobes as the structure responsible for the alpha-rhythm. In the Netherlands it was mainly the physiologist Ten Cate (a pupil of Pavlov) who performed very well designed animal studies on this subject (Ten Cate et al. 1939, 1940a, 1940b, 1940c). He concluded that the origin of the alpha-rhythm is not (completely) limited to the occipital cortex (at that time nobody made a distinction between the alpha-rhythm and the mu-rhythm) and that no rhythmic activity could be detected in subcortical areas, apart from a small amount of low-voltage fast activity.

Franke and co-workers remained faithful to Berger's ideas. He postulated that the thalamus has an inhibitory influence on cortical activity (Franke 1936, Van der Horst 1937, Franke and Koopman 1938, Franke 1939). Sleep was divided into two categories:

brainstem sleep and cortical sleep. Brainstem sleep, based on inhibition of the thalamus (resulting in desinhibition of the cortex and high EEG amplitudes) could be induced by barbiturates, hypoglycaemia or hypnosis. Cortical sleep (with cortical inhibition and a low amplitude EEG) was supposed to be the result of morphine- or ether-induced sleep. Epilepsy was seen as a paroxysmal exhaustion of the brainstem resulting in paroxysmal high cortical activity.

Before 1940 the clinical interest in the EEG remained mainly confined to problems in psychiatry and (sic) to parapsychologic phenomena. The EEG was considered to be "an absolutely reliable reproduction of pathological processes in the cortex" (Franke and Koopman 1938).

Schizophrenia, depression, hysteria and hypnosis were considered to be areas of prime interest. Franke (1942a,b) considered melancholia as a 'rigidity of the diencephalon'. If medication that was intended to stimulate the diencephalon (e.g., Benzedrine® intravenously) did not result in an activation of the thalamus (as shown by a depression of the alpha-rhythm), it was to be considered proof of a hypofunctional thalamus. Such a patient could be considered to be suffering from a primary depression and not from a secondary depression.

Barnhoorn (1941), who introduced the electroconvulsive shock treatment in the Netherlands in 1939, studied the EEG before and after convulsions induced by electroshock or by Cardiazol®. The problem was already formulated whether a clinically incomplete insult has the same therapeutic value as a complete insult when the induced EEG changes are the same. Despite his original preference for applications of the EEG in the fields of psychiatry and psychology, Franke postulated that "presumably the EEG is most promising in epileptic disorders" at a later date (Franke 1942a,b). In this he may have been influenced by the publications of Van der Horst (1941) en Van Gelderen (1941a,b). These publications provide a good impression of the state-of-the-art of neurology, neurosurgery and neurophysiology in 1940. Van der Horst described an eleven-year-old girl with a skull deformity on the left side due to forcipal extraction at birth. Frequent secondary generalised seizures started in the left hand with left-sided sensory pre-ictal signs. There were no neurological abnormalities and the ventriculogram was normal. The EEG, however, showed depression in the right frontal region and abnormal slow activity in the right parietal region. The (successful) operation by the neurosurgeon C. van Gelderen revealed a cicatrix on the right side just behind the Rolandic sulcus, its side having been defined by electrostimulation. Presumably, the cicatrix resulted from the second blade of the forceps (see also Van der Horst 1947).

The radiodiagnostic possibilities for the localisation of cerebral tumours were rather limited in the 1930s. Direct ventriculography had an understandably high morbidity in patients with supratentorial space-occupying lesions. As far as we know, Van Gelderen, abstaining from ventriculography, was the first to operate on patients with a cerebral tumour using the EEG as primary means for localisation (Van Gelderen 1941a,b). The sensitivity of the EEG in detecting cerebral tumours was estimated to range between 80 and 90 per cent (Van der Horst 1943).

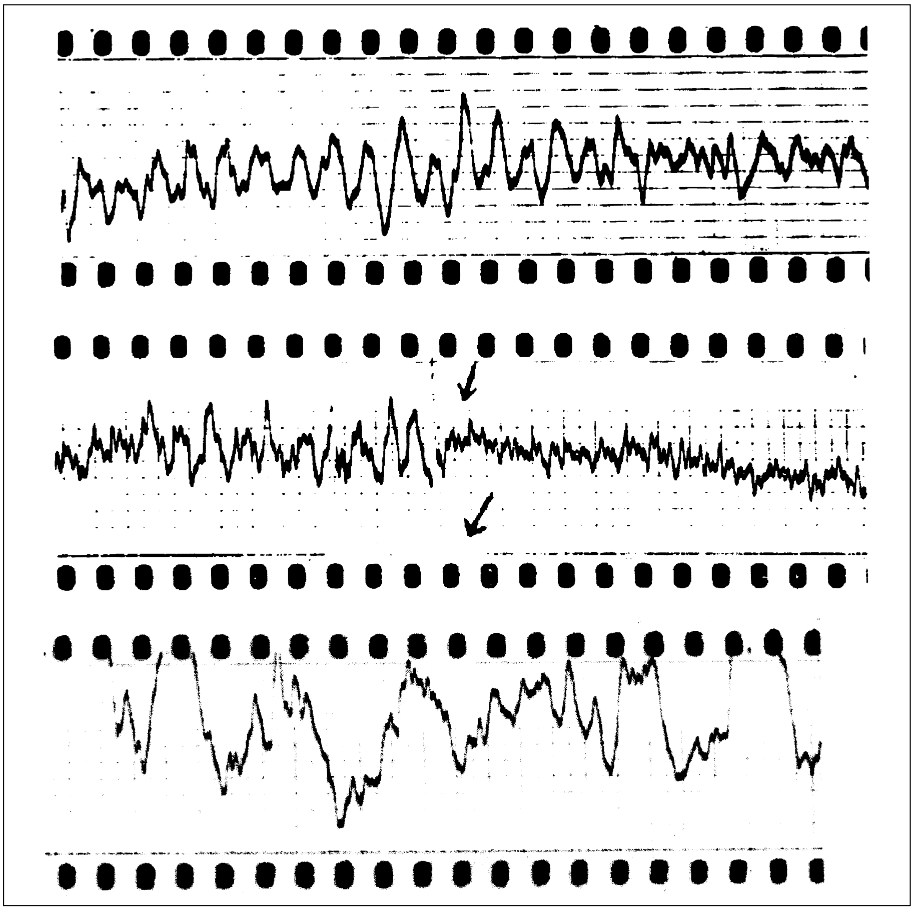

Figure 2.
Three examples from the first Dutch EEG study (Franke, 1936).
Upper trace: normal EEG (eyes closed).
Middle trace: suppression of the alpha rhythm during a light stimulus (starting shortly before the arrow).
Lower trace: EEG during barbiturate anesthesia.

Notwithstanding the considerable efforts by the Dutch pioneers mentioned above, the application of the EEG in clinical practice remained limited. EEG machines with more than one channel and a high common mode rejection as were already in use in the U.K. and in the U.S.A. (Matthews 1934, Walter and Camb 1936) were not built in the Netherlands. One can entertain two reasons for this. First, in the years before World War II, the Dutch scientific community was traditionally oriented to Germany and France and much less so to the Anglo-Saxon countries. Perhaps this explains why Koopman was not familiar with the superior Matthews design. Second, financial means for research purposes were limited because the economic depression that started in 1929 lasted longer in the Netherlands than in most other European countries. Nevertheless, the importance of the few Dutch pioneers was emphasised by the founder of electroencephalography, Hans Berger. In 1938, he published a list of the 75 most important EEG publications worldwide, a list which included four publications by Franke and Koopman (Berger 1938).

In June 1942, Franke published his Ph.D. thesis in which he reviewed his findings until then (Franke 1942a,b). In the same year, a first Dutch symposium was held on different aspects of the EEG (Ten Cate et al. 1943). After that, due to the German occupation, research in the Netherlands almost came to a complete standstill, which lasted until 1947, when a new generation of neurophysiologists had to start almost from scratch.

2 The period after 1945

This section describes shortly the development of clinical neurophysiological techniques in the Netherlands after 1945. Only a few names will be mentioned, mostly of those who introduced a new technique in the country. For the activities based on these innovations we limit ourselves to indicating the centres where most studies were done.

ELECTROENCEPHALOGRAPHY AND MAGNETO-ENCEPHALOGRAPHY

The potential of the EEG for objectivating epileptic disturbances had already been proven by Gibbs et al. in 1935, and the possibilities for using the EEG for the medical tests of military personnel were quickly recognised and became a stimulating factor for the development of modern EEG techniques (Gibbs et al. 1935). After the war there was a growing interest for the EEG in the Netherlands, not only for application in epileptic patients but also for the use in tumour diagnosis. In 1936, Walter and Camb had proved that the EEG could detect cerebral tumours and the EEG was sporadically used for this purpose by Dutch investigators before the war. However, the necessary EEG training could only be obtained overseas, for instance in Montreal (where J. Droogleever Fortuyn and O. Magnus received their training) or in Bristol (where W.G. Walter trained W. Storm Van Leeuwen).

After the return of these 'second generation Dutch electro-encephalographers' to their home country, clinical electroencephalography developed quickly in the Netherlands (Fig. 3) and reached, compared to many other countries, high standards. Positive factors were, among other things, the foundation of the Dutch Society for EEG and Clinical Neurophysiology in 1949, the well-organised training programme for EEG technicians, the interest of renowned Dutch physicists for clinical neurophysiology, and the start of Dutch factories for EEG machines (Elther, van Gogh).

After the introduction of multi-channel machines and transistors in the 1950s and 1960s, there were no real technical breakthroughs until the advent of digital techniques in the 1990s. However, there was a very active interest for new applications of the EEG in clinical practice beyond the customary indications. The importance of the EEG in the study of neonates was rapidly recognised (Academic Hospital Groningen), monitoring of the EEG during carotid surgery was initiated in 1960 (St. Anthonius Hospital Utrecht) and corticographies during epilepsy surgery were performed in the Ursula Clinic at Wassenaar and the Academic Hospital Utrecht from 1950 onwards. Sleep research was done in many centres (Academic Hospital Groningen, Epilepsy Clinic Heeze, Academic Hospital Amsterdam VU, Academic Hospital Leiden, Westeinde Hospital The Hague) and was stimulated by the introduction of an internationally accepted scoring system for sleep stages (Rechtschaffen and Kales 1968).

Animal research, aimed at the origin of the rhythmic activities in the brain, which was started in the Institute of Medical Physics (Utrecht) by W. Storm van Leeuwen and F.H. Lopes da Silva, proved to be the beginning of a highly important and continuous line of research.

As described in the previous paragraph, manual Fourier analysis of the EEG signal was carried out by Koopman as early as 1938. In the same year, Grass and Gibbs (1938) published their design for a more or less automatic machine for EEG frequency analysis. The first clinically applicable analogue frequency analysers were introduced in the 1950s. However, EEG quantification really started with the introduction of digital computers (which were extremely costly at that time) in 1968. W. Storm van Leeuwen and O. Magnus in particular advocated the use of EEG computers in a clinical setting. Dutch studies of computer analysis of the EEG since that time have been directed, amongst others, at metabolic brain disease (Academic Hospital Rotterdam), cerebrovascular disease (Ursula Clinic Wassenaar, Academic Hospital Utrecht), neurotoxicity (Westeinde Hospital the Hague), monitoring during vascular surgery (Anthonius Hospital Nieuwegein, Academic Hospital Utrecht) and epilepsy (Epilepsy Clinics Heemstede and Heeze). Van Huffelen proved that computer analysis of the EEG could reveal clinically important abnormalities in EEGs that had been considered normal on visual assessment (van Huffelen 1984).

The introduction of digital techniques for data acquisition and storage has given a new stimulus for electroencephalography. The problem of huge EEG archives became manageable, post hoc changes in data presentation became possible, and the use of a large number of electrodes, necessary for dipole analysis in selected cases, became feasible (Academic Hospital Utrecht). The handling of the tremendous amount of EEG data in epilepsy clinics and sleep centres would not have been possible without modern digital storage media.

Finally, it should be mentioned that several Dutch scientists made important contributions to the development of non-linear analysis methods of the EEG (Lijenburg Hospital the Hague, Epilepsy Clinic Heemstede, Academic Hospital Amsterdam VU).

The history of the EEG in the Netherlands can be summarised as follows: after a late start, the number of EEG recordings rose rapidly, reaching a maximum around 1979, followed by a quantitative decline caused by the emergence of CT and MRI. At the time of writing, the most important remaining strong points of the EEG are the measurement of primary functional disturbances of the central nervous system

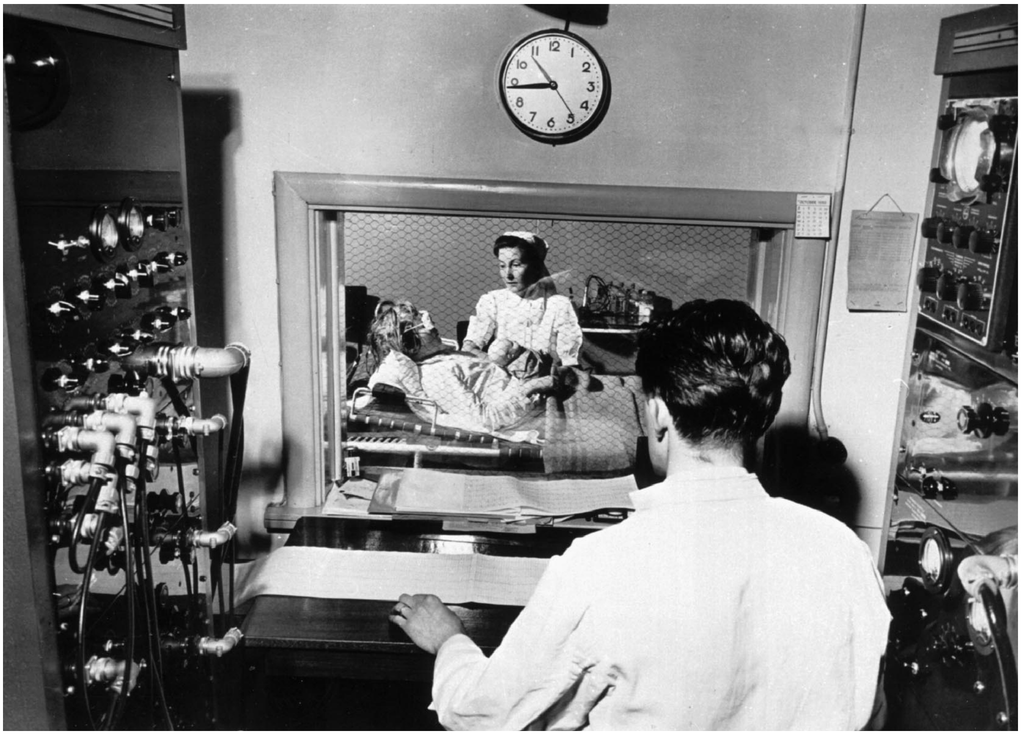

Figure 3.
EEG registration in 1949: the technician is sitting 'in' the EEG machine (an Offner Dynograph). The same machine was used for EMG. For this application an oscilloscope was added (top right).

(epilepsies, cognitive disorders, CNS damage in neonates), monitoring in the operating room and on intensive care wards, and the evaluation of sleep/wake disorders.

Experiments with magneto-encephalography (MEG) have been performed in the Netherlands since the 1980s (Twente University). In 1996 a joined effort was made by the Royal Academy of Sciences and several departments of Clinical Neurophysiology to start a Dutch centre for magneto-encephalography. A 165-channel machine was installed at the Academic Hospital of the Vrije Universiteit in Amsterdam. At the time of writing, the clinical potential of this new technique is not completely defined. Without doubt the high resolution in the spatial as well as in the frequency domain of magneto-encephalography provides unique research possibilities. It is relatively easy to combine MEG data with anatomical MRI data and to use these data in neuronavigation apparatus. However, as with the MRI apparatus, the accessibility of the MEG for severely ill patients is limited. For the time being, the most important applications of the MEG are the three-dimensional localisation of epileptic foci, the pre-surgical localisation of cortical fields and the study of activities in the brain that require a higher time resolution than fMRI, PET or SPECT can provide.

ULTRASOUND AND CIRCULATION MEASUREMENTS WITH RADIOACTIVE ISOTOPES

In 1955 Leksel described the use of ultrasound for determining the position of the 'mid-line structures' of the brain, which was later proven to be a reliable technique. De Vlieger (Academic Hospital Rotterdam) introduced this *echo-encephalography* in the Netherlands, made several improvements and found new applications. The limited training necessary for echo-encephalography, the low cost and the non-traumatic nature of echo-encephalography resulted in its widespread use. However, after the introduction of the CT in the Netherlands (1975) the 'echo' gradually disappeared. From having once been a sometimes life-saving technique, echo-encephalography has now become obsolete in neurological practice.

The frequency shift predicted by Doppler (Doppler 1842) was confirmed experimentally for the first time by the Dutch scientist Buys Ballot (Buys Ballot 1845). During the 1960s, apparatus for the transcutaneous measurement of blood flow velocities in man were constructed. The first Dutch publication in this field appeared in 1970 (Melis-Kisman and Mol 1970). Age-dependent normal values of systolic and diastolic flow velocity values in the common carotid artery, the vertebral artery and the brachial artery were presented in Mol's thesis (Mol 1973), and subsequently used by many departments of clinical neurophysiology. This *haematotachography* was certainly useful in the hands of experienced examiners for improving the indication for angiography. However, the method had the essential drawback that anatomical information was missing and that therefore the increase in flow velocity at the site of a stenosis could be easily missed. Nowadays, continuous wave Doppler has only limited applications.

In 1974 the first combination of an anatomical 'B-scan' and a pulsed Doppler system was realised by Barber (Barber et al. 1974); the first commercial apparatus becoming available in 1980. In the Netherlands the use of the *Duplex scanner* for the detection of stenosis in the carotid artery system was advocated by Breslau. He described normal range values and the clinical importance in several publications and a thesis (Breslau 1982). In addition, Ackerstaff studied the possibilities and limitations of the Duplex scanning for the vertebral arterial system (Ackerstaff 1985). Since that time technical improvements have been such that in selected cases it appears possible to abstain from angiography before carotid endarterectomy. At the time of writing, the relative merits of different methods for detecting carotid artery disease are yet undecided. Without tabulating all the pros and cons in this ongoing discussion, it is worth mentioning the most important advantages of Duplex scanning, which are the complete non-traumatic nature and the low cost, and the main disadvantage, which is the necessary manual dexterity that is not within everybody's reach.

Transcranial Doppler (TCD) recordings (Aaslid 1982) have been used mainly for the detection of vascular spasms after subarachnoidal haemorrhage, and for the detection of subcritical flow and the occurrence of emboli during carotid endarterctomy. TCD also gives the opportunity to study the vascular changes and the vascular 'reserve capacity' before, during and after carotid surgery (Academic Hospital Utrecht). The indications for this technique may widen in the near future now that transcranial Duplex scanning has become technically feasible.

The original *cerebral blood flow* (CBF) measurement with N_2O (Kety and Schmidt 1945) was difficult to apply in patients. Clinical application became possible after the introduction of Kr^{85} as a radioactive tracer (Lassen et al. 1963). In the Netherlands, CBF measurements were mainly taken in the Ursula Clinic at Wassenaar and, at a later date, in the Westeinde Hospital in The Hague. These studies were originally directed at vascular changes in the acute phase of a cerebrovascular accident and in the periphery of space occupying lesions (Mosmans 1974). When a new method using inhaled Xe^{133} became available, follow-up studies could be performed in the period after a CVA or a carotid endarterectomy had been carried out. These studies with radioactive isotopes have increased the knowledge of disturbances of the cerebral circulation greatly. The hyperperfusion syndrome, the ischemic penumbra, disturbed autoregulation and intra-cerebral steal syndromes became known entities thanks to the experience with isotope studies. However, the method remained essentially a two-dimensional approach with a limited spatial and temporal resolution. Advances in SPECT and above all PET technology have made the krypton and xenon techniques obsolete.

ELECTROMYOGRAPHY AND NEUROGRAPHY

In the nineteenth century Von Helmholz succeeded in measuring the conduction velocity of the ulnar nerve (von Helmholtz 1870). The concept of the motor unit was described by Sherrington in 1924, and Adrian used a concentric needle electrode as early as 1929. Nevertheless, it was 1952 before the first Dutch publications on *electromyography* (EMG) appeared. In that year a twin publication appeared on the construction of an electromyograph (Den Hartog et al. 1952) and its clinical uses (Lorentz de Haas 1952). The basic principles of electromyography, such as spontaneous muscle fibre activity, sprouting and polyphasic motor unit potentials, were already well known at that time.

Routine measurement of *motor and sensory conduction velocities* only became feasible after the introduction of modern amplifiers from 1960 onwards (Fig. 4).

The introduction of 'single fibre myography' (Stålberg et al. 1971) and stimulated 'single fibre myography' made endplate studies possible in all major centres for clinical neurophysiology. More specialised techniques such as 'macro-EMG remained limited to a few academic hospitals.

Over the years, many Dutch publications have appeared on *reflex studies*. Brainstem reflexes and Hoffman reflexes were studied by Ongerboer de Visser (Ongerboer de Visser 1976); quantification of peripheral reflexes was reported by Rico, among others, (Rico and Jonkman 1982). Measuring *muscle fibre velocity* can be considered another specific Dutch field of interest. A clinically applicable method was developed in the Groningen Academic Hospital (Zwarts 1989).

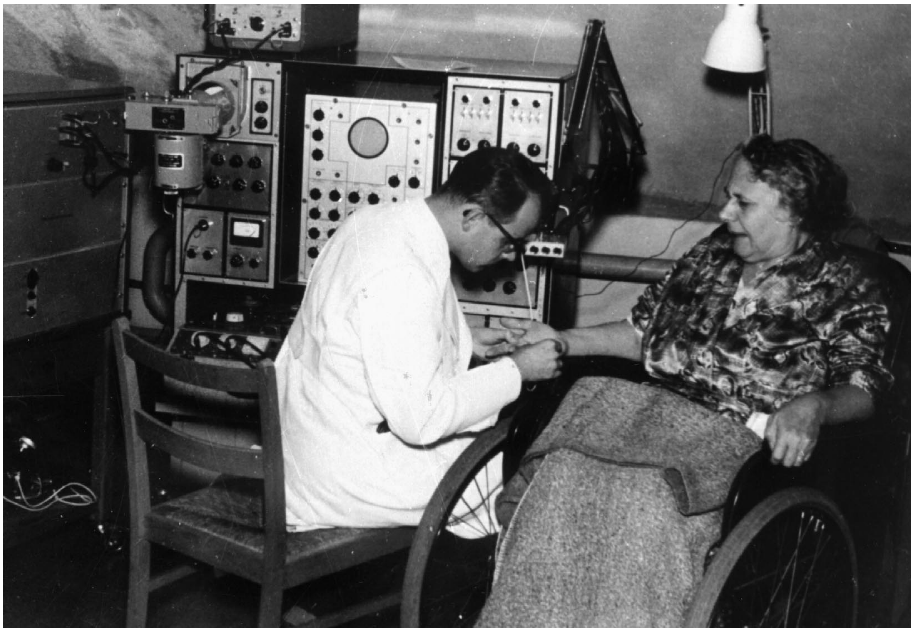

Figure 4.
Myography in 1963: the apparatus is still complex and the technical possibilities are limited. The resident (in training for his clinical neurophysiology license) is H.J.G.H. Oosterhuis who in later years became professor of Neurology in Groningen.

Surface EMG has played a role in rehabilitation medicine but has had only minor usage for the neurological patient. However, recent developments using multi-electrode arrays (Academic Hospital Nijmegen) make new applications possible in the near future.

Another recent development is *neuronography*: the registration of the action potentials of single nerve fibres (Academic Hospital Utrecht). This technique is probably of limited use for neurological patients but has already played an important role in the study of hypertensive disease.

The EMG has been used as a major diagnostic item in many Dutch *clinical studies*. Although many publications could be mentioned here, we will limit ourselves to one example. EMG made it possible to demonstrate that the incidence of 'critical illness polyneuropathy' on intensive care wards is much higher than can be diagnosed by clinical observation (Leijten 1996). This finding is of considerable importance for the prognosis of the individual patient.

It is difficult to estimate the future clinical importance of the EMG. Improved immunological and genetic testing have limited the use of the EMG in some specific fields. On the other hand, EMG has proven to be the most important tool in the quantification and categorisation of peripheral nervous system disease.

EVOKED POTENTIALS

The first Dutch study on *visual evoked potentials* (VEP) was published by Van Hof (Van Hof 1958), who constructed visual averaged evoked potentials by manually adding EEG signals. In 1960 the first dedicated computer became available (Mnemotron Computer of Average Transients). Speckreijse analysed transfer functions in the central nervous system (Speckreijse 1966) of visual evoked potentials; Jonkman studied normative values and clinical usefulness (Jonkman 1967). Van der Tweel received international credit for his idea to use (sinusoidal) modulated light instead of flashes for retinal stimulation (Van der Tweel 1958, Kamphuisen 1969). At the moment there are only a few indications left for the clinical use of visual evoked potentials: the detection of demyelinating lesions in the optic nerve (Halliday 1973) and the assessment of the visual system in (premature) infants.

The use of *somatosensory evoked potentials* (SEP) was introduced in the Netherlands by Posthumus Meyes (1969). The (anatomical) origin of the main SEP components was studied in the Academic Hospital Utrecht. Just like for the VEP, the indications for the clinical use of the SEP has become more strictly defined in the last decennium. At the moment the SEP is considered to be of importance for the prognosis in patients with severe traumatic or ischemic brain injury (Heerlen, Amsterdam AMC), before and during surgery for brachial plexus laesions, presurgical localisation of the sensory cortex (Academic Hospital Vrije Universiteit, Academic Hospital Utrecht), in detecting silent laesions in demyelinating disease, and as a monitor during spinal, medullar or aortic surgery.

Shortly after the first descriptions (Kiang 1961, Jewett et al. 1970) of *brainstem auditory evoked potentials* (BAEP), Dutch scientists became active in this field. Since it was apparent that objective quantification of hearing thresholds would be an important indication for the BAEP, determining normative values in (preterm-) neonates was of primary importance (Rotteveel 1986). At the time of writing, it is not clear whether (fully automated) brainstem evoked potential measurements will replace the Ewing test in the near future. Apart from this the BAEP can play an important monitoring role during brainstem surgery. In patients with severe brain trauma the disappearance of the BAEP remains an important negative prognostic sign.

Middle and long latency auditory evoked potentials had until recently no clinical importance. However, the possibilities of high-resolution EEG and MEG have made pre-surgical anatomical localisation of the relevant brain structures of the auditory system possible.

The introduction of magnetic stimulation (Barker et al. 1986) made it possible to use *motor evoked potentials* in daily practice. Using this technique cortical excitability (e.g., in migraine) and conduction velocity in the pyramidal tracts can be measured (Heerlen, Leijenburg Hospital the Hague). The use of motor evoked potentials as a monitor during aortic surgery resulted in a considerable decrease in neurological complications (Amsterdam AMC).

Cooper et al. (1962) were the first to describe a late *event related potential* (ERP), the contingent negative variation. The clinical use of such ERPs is rather limited, but many excellent psychophysiological studies have been carried out in the Netherlands using this technique, mainly by Brunia and co-workers (Breda, Katholieke Universiteit Brabant).

The list of neurophysiological techniques mentioned above is certainly not complete. We have limited ourselves to the techniques that are more or less exclusively the competence of neurophysiologists. Nystagmography and retinography, for example, are performed by neurophysiologists in some hospitals, in other centres by ENT specialists or ophthalmologists. Overlapping fields have often given rise to 'border incidents' between different professional groups. Fortunately, there is a tendency in favour of cooperation rather than competition. We know of several instances where different groups use the same equipment and share their know-how.

3 The Dutch Society for Electro-encephalography and Clinical Neurophysiology

The Dutch Society for Electro-encephalography and Clinical Neurophysiology was founded in 1949 and renamed as the Dutch Society for Clinical Neurophysiology in 1980. Unfortunately the first minutes have not been saved; a list of members from 1952 is the oldest item still present in the archives of the Society. At that time there were 46 members (compared to 310 in 1999).

The Society has several foreign and Dutch honorary members: H. Gastaut (†), M.A.B. Brazier (†), O. Magnus, W. Storm van Leeuwen, S.L. Visser and F.H. Lopes da Silva. In addition, Mrs. Brazier received an honorary doctors degree from the University of Utrecht in 1976.

In 1992 it was decided to found a Dutch award for excellent clinical neurophysiological research: the 'Storm van Leeuwen-Magnus award' (Fig. 5). Successive laureates were M.J. Zwarts (1992), D. Stegeman (1996) and F.H. Lopes da Silva (2000).

Training of EEG technicians has always been an important issue for the Society. Originally the Society took care of all aspects of this training programme; in later years it was done in close collaboration with the Dutch Society of Clinical Neurophysiology Technicians. Although a commercial educational institution is now responsible for the distribution of teaching matter and the organisation of exams, the contents of the course for technicians, which lasts three years, remain the responsibility of a combined committee of both Societies.

Quality control has been implemented since 1977. At that time, a committee (chairman S. Boonstra) of the Society reported on the quality of EEG registrations and on the reports of a large number of departments for clinical neurophysiology. More recently, quality control –including site visits of 'non-teaching departments' – has been done in collaboration with the Netherlands Society of Neurology while the supervision of teaching departments remains under jurisdiction of the Medical Specialists Registration Board.

Advanced courses for qualified neurophysiologists and technicians have been organised since 1981. At least one course is planned each year. Examinations for neurophysiological residents and neurophysiologists started in 1990.

In 1990, at the time of the fiftieth anniversary of the Society, it was decided to combine almost all activities of the Society (scientific meetings, advanced courses, business meetings) in a yearly session of two days. This initiative proved to have a positive influence on the attendance.

Since 1947 several members of the Dutch Society have served as officers for the International Federation of Societies for EEG and Clinical Neurophysiology (W. Storm van Leeuwen, O. Magnus, B.W. Ongerboer de Visser, A.W. de Weerd) or as members of the editorial board for the *Journal of Electroencephalography and Clinical Neurophysiology* (W. Storm van Leeuwen, O. Magnus, H. van Duijn, F.H. Lopes da Silva, E.J. Jonkman and C.H.M. Brunia).

Since 1973 five international congresses on (or related to) clinical neurophysiology have been organised in the Netherlands:

- The 2nd World Congress on Ultrasonics in Medicine (Rotterdam).
- The IX. World Congress on EEG and Clinical Neurophysiology (Amsterdam).
- The 3rd European Congress on EEG and Clinical Neurophysiology (Amsterdam).
- The 3rd International Congress on Brain Electromagnetic Topography (Amsterdam)
- The 11th International Symposium on Cerebral Hemodynamics (Zeist).

The largest of these congresses (Amsterdam, 1977) assembled 1244 active participants from all over the world.

Figure 5.
Two key-figures of clinical neurophysiology in the Netherlands after 1948: Prof. W. Storm van Leeuwen (left) and dr. O. Magnus (right) with an example of the Dutch neurophysiology award that was named after them (Utrecht 1992).

Official qualification for clinical neurophysiologists started in 1957. From that time onwards it was possible to obtain an 'EEG endorsement' on the board registration (for neurologists as well as for psychiatrists). However, the possibilities for electrophysiological training during one year within the neurological curriculum remained unsatisfactory. In 1982 a complete separation of neurologists and neurophysiologists was proposed by the executive board of the Society but ultimately rejected by the majority of the members. In 1991 two separate curricula were introduced: one for the clinical neurologists ($4\frac{3}{4}$ years of neurology, $1\frac{1}{4}$ years of clinical neurophysiology) and one for clinical neurophysiologists ($3\frac{1}{2}$ years of neurology, $2\frac{1}{2}$ years of clinical neurophysiology).

4 Neurophysiological publications and doctoral theses

It is impossible to give a survey of all neurophysiological publications by Dutch authors. As an anecdote it might be mentioned that J. ten Cate and W. Storm van Leeuwen were the first to publish their findings in the then newly founded *Journal of Electroencephalography and Clinical Neurophysiology* (Ten Cate et al. 1949, Storm van Leeuwen 1950).

The publishing activity of the present generation of Dutch neurophysiologists as compared to colleagues from other countries can be demonstrated by the data presented in Table I. In this table the number of manuscripts submitted to the editor-in-chief of the *EEG Journal* from all European and Asian countries (with the exception of Japan) is given for a period of four years (data courtesy of Prof. P. Rossini, editor-in-chief). Only data from the five most active countries are presented.

Table I.

	Germany	Italy	U.K.	Netherlands	France
1996	46	35	17	13	15
1997	63	52	31	24	23
1998	53	56	19	12	12
1999	62	54	18	24	20
Total	224	197	85	73	70

However, one has to realise that the *EEG Journal* is only one of the many journals in which Dutch publications on neurophysiology have appeared. Moreover, manuscripts have not only been accepted by medical journals, they can also be found in mathematical journals or journals for applied physics. The total of Dutch neurophysiological publications in the second half of the last century remains as yet an unexplored 'bibliometric' field.

An insight into the progress of neurophysiological research in the Netherlands can also be obtained by studying a chronological list of doctoral theses on neurophysiological subjects. Limiting ourselves to those theses that were supervised by a professor in clinical neurophysiology or that were mainly dedicated to a neurophysiological subject, we could collect 145 theses, starting with Franke (1942). However, such a list is open to criticism: it is not always possible to categorise the theses in neurological, psychiatric, neuropsycholocical and neurophysiological. Indeed, it would be a *testimonium paupertatis* for the Dutch neurosciences if such a distinction could be made in all cases! A subdivision of the 145 theses mentioned above is given in Table II.

Table II.

Neurophysiological subjects s.s.		**85**
EEG	14	
Sleep research	10	
EMG + reflex studies	26	
VEP	8	
SEP	5	
(B)AEP	3	
MEP	3	
ERP	1	
Ultrasound/circulation	15	
Neurophysiology in neurological or psychiatric disease		**37**
Neurophysiology and rehabilitation medicine		**4**
Miscellaneous		**19**
Total		**145**

For a small country the number of doctoral theses on neurophysiological subjects over a time span of fifty years seems rather satisfactory. Most subjects studied were quite up to date in view of the international scientific developments (see previous section). The division between more basic research and development of new techniques for clinical practice on the one hand and the participation in clinical studies on the other (see Table II) is well balanced. Notable is the Dutch interest for aspects of the cerebral circulation, evoked potentials and sleep research.

Finally, one, perhaps typical Dutch, aspect should be mentioned. In the list of theses we encountered numerous examples where a thesis was not prepared in an academic hospital but where the necessary studies were done and direct supervision was given in a non-academic teaching hospital.

TEACHING DEPARTMENTS

The Dutch neurophysiologists who did their advanced training abroad shortly after World War II were fortunate to do so in EEG departments which had and still have very high standards not only for research but for 'routine' clinical studies as well (Bristol, Montreal, Paris). As a result, from the very beginning priority was given to the optimisation of the quality for recording and interpretation of EEGs. It was thought necessary to train neurologists for at least one year in electro-encephalography before they could be entrusted with the responsibility of running their own departments. Nowadays this may seem a little bit overdone since, even though at present the training takes 15 months, it includes not only EEG but also EMG, evoked potential recordings, monitoring during surgery and on intensive care wards, recording in premature infants, etc. However, one should realise that the clinical responsibility in the 1940s and 1950s was, at least for the interpretation of the EEGs, very high because of the limited availability of other diagnostic means. Nevertheless, it took until 1957 before an official status for clinical neurophysiologists was obtained. After that time only those neurologists, who had trained for one year in a teaching department for clinical neurophysiology recognised by the Medical Specialist Registration Board, were allowed to practice clinical neurophysiology. From 1957 until 1991 this recognition could only be obtained by those neurologists who were inclined to practice part-time or full-time clinical neurophysiology. Since a considerable percentage of neurology residents were not interested in doing so the number of teaching facilities could remain limited. After 1991, when clinical neurophysiology became a mandatory item for all neurological residents, it was necessary to have the number of teaching departments equal to the number of teaching hospitals for clinical neurophysiology. The present teaching departments are tabulated below. For each department we tried to establish the year in which official recognition as a teaching department was obtained but it turned out that this information was no longer available. All dates are between 1957 (e.g., Academic Hospital Utrecht and Ursula Clinic in Wassenaar) and 1998 (Enschede). Because of the uncertainty of the recognition dates we will mention all department heads over the years for the 16 present teaching departments. For the academic hospitals we have also listed the academic appointments of the department heads. We realise that such a list does injustice to the medical and non-medical staff members of the teaching departments. To obtain a licence as a teaching department it is mandatory to have, amongst many other things, a full-time physicist as a staff member. These physicists have played a very important role in the high quality of clinical care that is achieved nowadays and were crucial in the research programmes of these departments.

Amsterdam: Academic Hospital University of Amsterdam

Prof. dr. J. Drooglever Fortuyn	1949 - 1951		
Drs. W.J.M. Hootsmans	1951 - 1985		
Prof. dr. B.W. Ongerboer de Visser	1985 - 2001	professor	1988

Amsterdam: Academic Hospital Vrije Universiteit

Dr. H. Herngreen	1953 - 1964		
Prof.dr. S.L. Visser	1964 - 1989	ass. professor	1967
		professor	1973
Dr. R.L.M. Strijers	1989 - 1993		
Prof.dr. E.J. Jonkman	1993 - 2000	professor	1994
Prof.dr. C.J. Stam	2000 -	professor	2000

Amsterdam: Sint Lucas/Andreas Hospital

Prof. dr. G.P.M. Horsten	1966 - 1967
Dr. A. Kropveld	1967 - 1973
Dr. A. Zonneveldt	1973 - 1983
Dr. B.W. Ongerboer de Visser	1983 - 1984
Dr. H. van Duijn	1984 -

Enschede: Medisch Spectrum Twente

Drs. H.M. Greebe	1965 - 1989
Drs. J.G. Wilts	1989 -

Groningen: Academic Hospital

Dr. H.K.G. Bartstra	1949 - 1953		
Dr. A.M. Hamoen	1953 - 1962		
Dr. E. Hiddema	1962 - 1964		
Prof. dr. S. Boonstra	1964 - 1994	ass. professor	1973
		professor	1980
Dr. T.W. van Weerden	1994 -		

Den Haag : Hospital Zuidwal / Leijenburg

Dr. C. Goor	19xx - 1986
Drs. H. Morré	1986 - 1991
Drs. D. Tavy	1991 -

Heerlen: De Wever Hospital/ Atrium Medisch Centrum

Dr. J.F.M. Mol	1957 - 1981
Dr. F. Spaans	1981 - 1987
Dr. J.W. Vredeveld	1987 -

Leiden: Academic Hospital

Dr. W. Storm van Leeuwen	1948 - 1959	ass. professor	1957
Dr. K. Mechelse	1959 - 1970		
Prof. dr. H.A.C. Kamphuisen	1972 - 1994	ass. professor	1971
		professor	1980

Prof. dr. J.G. van Dijk	1994 -	professor	2001
Maastricht: Academic Hospital			
Prof. dr. J.F.M. Mol	1957 - 1985	professor	1978
Prof. dr. F. Spaans	1985 -	professor	1985
Nijmegen: Academic Hospital St. Radboud			
Drs. P.J.H. Bernsen	1955 - 1969		
Prof. dr. S.L.H. Notermans	1969 - 1996	ass. professor	1969
		professor	1979
Prof. dr. M.J. Zwarts	1996 -	professor	1996
Nijmegen: Canisius / Wilhelmina Hospital			
Drs. P.J.H. Bernsen	1955 - 1956		
Drs. P.J.H. Bernsen	1961 - 1986		
Dr. W.I.M. Verhagen	1986 - 1998		
Dr. J. Meulstee	1998		
Rotterdam: Academic Hospital			
Dr. B.G. Ziedses des Plantes	1952 - 1954		
Prof. dr. M. de Vlieger	1954 - 1985	ass. professor	1970
		professor	1980
Dr. K. Mechelse	1985 - 1991		
Dr. R.J. Schimsheimer	1991 - 1993		
Dr. J. Meulstee	1993 - 1998		
Dr. G.H. Visser	1999 -		
Tilburg: St. Elisabeth Hospital			
Dr. M.P.A. de Grood	1951 - 1952		
Drs. J.J. van Luijk	1952 - 1985		
Drs. R.L.L.A. Schellens	1985 -		
Utrecht: Academic Hospital			
Prof. dr. W. Storm van Leeuwen	1951 - 1985	professor	1972
Prof. dr. A.C. van Huffelen	1985 -	professor	1985
Utrecht / Nieuwegein: St. Antonius Hospital			
Dr. A.R. Simons	195x - 1983		
Dr. R.G.A. Ackerstaff	1983 -		
Wassenaar: Ursula Clinic / den Haag: Westeinde Hospital			
Dr. O. Magnus	1949 - 1979		
Dr. E.J. Jonkman	1979 - 1993		
Dr. A.W. de Weerd	1993 -		

Closing remarks

In the previous sections we have outlined the history of clinical neurophysiology in the Netherlands since 1936. The reader might be slightly disappointed that scientific achievements since 1947 have not been described in detail. There were three main reasons for not doing so. First, it would be a time-consuming undertaking to analyse all Dutch publications since 1947. Second, it seemed incorrect to pass judgment on the work of clinical neurophysiologists who are still active in the field or who have retired only recently. Third, when studying the titles of the many theses produced by clinical neurophysiologists in the second half of the twentieth century, we realised that a lot of work had been done in the past that was at that time important for clinical practice and better understanding of physiological mechanisms, but which is outdated from the present point of view.

Even when we abstain from trying to draw up an inventory of the total scientific output it is possible to indicate some main areas of interest, however, this choice is only based on this writer's personal experience and can be challenged. Over the whole period between 1949 and 2000 the study of *vascular disturbances* has been pursued in the Netherlands, starting with EEG studies in the 1940s, continuing with ultrasound and isotope techniques, with computer analysis of patients with minor ischaemic disturbances, with the development of sophisticated monitoring techniques and even at the present day with the evaluation of ischaemic events in (premature) newborn infants. The second EEG line of research over the same period is the *epilepsy-related research*. In this, our country had the special advantage of having three epilepsy centres of high standing.

When considering more or less specific Dutch fields of interest in myography, three items come to mind: first, the many publications on *brainstem reflexes* and, to a lesser degree, peripheral reflexes; second, the studies on *models* of nerve action potentials and *muscle fibre conduction*; and third, the many clinical studies on afflictions of *peripheral nerves* in which clinical neurophysiology played an important role.

Regarding evoked potentials the stimulation modes advocated by van der Tweel c.s. and the *event related potential studies* come to mind as being of lasting importance.

The last item that could be mentioned (but once again, this is a personal choice) is the research of *sleep/wake disorders* in which several Dutch centres have been active from the 1950s onwards.

It goes without saying that indications for clinical neurophysiological diagnostics have changed and have become on the whole less numerous since the introduction of CT, PET, MRI and fMRI. On the other hand, from the international literature and from experience in our own country we know that there have been many important neurophysiological breakthroughs in recent years, such as (limiting ourselves to the EEG): advanced methods of source localisation, prediction of seizures, the detection of non-linear structure underlying brain signals, and the continuous monitoring of IC patients. This implies that in our view clinical neurophysiology will remain an essential part of the neurological sciences for many years to come.

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Child Neurology 12

W.O. Renier

In 1968, Droogleever Fortuyn, professor of Neurology at the University of Groningen, supported by his colleagues Biemond (University of Amsterdam) and Sillevis Smitt (University of Utrecht), took the initiative to start a section of Child Neurology as a special field of interest of the Netherlands Society of Psychiatry and Neurology. The first meeting was held in October 1969 in Amsterdam.

This initiative allowed three young specialists, Cobus Willemse (Neurology, Utrecht), Paul Fleury (Neurology, Amsterdam) and Peek Le Coultre (Neurology, Groningen) to present themselves as the delegates of the Dutch Child Neurology Section at the 7th Oxford Meeting of the Spastic Society of Great Britain (1970).

The Oxford Meetings had their origin in the Study Group of the Medical and Information Unit of the Spastic Society of Great Britain. In 1958 the president of this study group, the pediatrician Ronald Mac Keith (1908-1977) from London, was a prominent advocate of a subspeciality of Child Neurology. At the 7th Oxford Meeting, the Oxford Study Group was transformed into the European Study Group on Child Neurology and Cerebral Palsy, which subsequently became the European Federation of Child Neurology Societies (EFCNS). Within the organisation of the EFCNS, Dutch childneurologists have played a prominent role. The biannual European congress of the EFCNS has been organised twice by the Dutch Child Neurology Society in the Netherlands (Noordwijkerhout, June 13-17, 1983, and Maastricht, October 8-11, 1997).

The International Child Neurology Association (ICNA) was established in 1973. During the first congress of the ICNA in Toronto (1975), the idea emerged to found a scientific society that accepted neurologists as well as pediatricians as members. The idea implied that the Section of Child Neurology, being a non-autonomous body within the Netherlands Society of Neurology, had to be replaced by a new and autonomic organisation. Such a proposition was forwarded at the autumn scientific meeting of the Section in Nijmegen and carried by the majority of the members. After years of preparation by Paul Fleury, Peter Barth, Boudewijn Peters and Christa Loonen, and many years of discussion with the Board of the Netherlands Society of Neurology, the Dutch Child Neurology Society was officially founded in 1980. The first president was professor Willemse (Utrecht). The first mission of the new society was to give the new organisation a large and independent financial basis. To implement that, any medical and non-medical person working in healthcare offices for infants and children and interested in childneurology, could become a member of the society, but only full-time active childneurologists could be a member of the board. In 2000, the Dutch Child Neurology Society had 290 members.

After a dynamic start of child neurology departments in the university hospitals of Utrecht, Nijmegen and Groningen, other such departments followed in Amsterdam, Rotterdam, Leiden and Maastricht. In 2000, each Dutch university hospital commanded a childneurology department and two to four members of staff. In the last decennium, most of these departments, which started in the departments of Neurology, have been integrated in the departments of Pediatrics.

A milestone in the profile of the new section of Child Neurology was the organisation of a two-day course on child neurology (Boerhaavecursus over Kinderneurologie, Leiden, May 25- 26, 1972,), at which the most important aspects of the pathology of the developing central and peripheral nervous system were presented. The course was a resounding success (there were 464 participants) and resulted in a handbook on child neurology (Willemse 1973). In subsequent years, the Dutch Society of Child Neurology organised many symposia and training sessions.

From the beginning, Willemse invited the members of the Section to his department in Utrecht once a month. These so called 'tea club' meetings were a forum for the presentation and discussion of exceptional cases or cases pro diagnosi.

Every year since 1973, an autumnal symposium is organised by one of the university child neurology departments. The theme of the symposium is generally determined by the research interest of the organising department. Since the 1980s, two meetings have been organised each year: one the autumnal symposium with a predominantly educational aspect; the other a springtime meeting in a regional general hospital where case reports and results of scientific research by members of the Society are presented and discussed.

An annual training course (Cursorium) for residents in neurology or pediatrics was initiated in 1995 in order to stimulate their interest in child neurology and to promote cooperation between the two disciplines in an early phase of their training.

The Cornelia de Lange prize was instituted in 1992. Cornelia Catharina de Lange (1871-1950) was professor in Pediatrics at the University of Amsterdam and had a particular interest in diseases of the central nervous system. The prize is awarded to child neurologists who achieve outstanding merits in child neurology.

Child neurology versus neuropediatrics

In the Netherlands, child neurology is a discipline, practised in the majority of the cases, by neurologists with a special interest in child neurology and neuropathology. In many other countries, pediatricians constitute the majority and call themselves 'neuropediatricians'. The first generation members of the Dutch Child Neurology Society were the neurologists Cobus Willemse and Jaap Troost (Utrecht), Peek Le Coultre and Ko Begeer (Groningen), Christa Loonen (Rotterdam), Fons Gabrëels and Willy Renier (Nijmegen), Boudewijn Peters (Leiden), Paul Fleury and Charles Njiokiktien (Amsterdam) and Wim Feikema (Rotterdam, later Deventer), and the pediatricians Peter Barth (Amsterdam) and Nan Krijgsman (Nijmegen).

The pioneers of the first period intended to make child neurology an officially recognised (sub-) specialism in the Netherlands with scientific input from both neurology and pediatrics. For many years, neither the Society of Neurology nor the Society of Pediatrics was willing to accept this proposition. The board of the Society of Pediatrics was unwilling to accept that non-pediatricians should take care of children. Because approximately one third of the patients in pediatric departments are children with neurological signs and symptoms, the first child neurology departments in Utrecht, Nijmegen and Amsterdam were perceived as a dangerous development. The situation in Nijmegen was illustrative of the turf battle between the two mother disciplines. At the University Hospital Nijmegen, there were two departments, a child neurology department at the Institute of Neurology and a neuropediatric department at the Institute of Pediatrics. In 1977 Gabrëels and Renier wrote a letter proposing a fusion of the two departments, however, this proposal met with a rebuttal by the heads of both Institutes. It was 1986 before the idea to create one unit could be realised, and even then it needed the prior concession of the Institute of Neurology to accept that the interdisciplinary unit would reside in the Pediatric Clinic and that the chair of Child Neurology of the Institute of Neurology would be disconnected from its foster mother. At the national level, it took even longer to reach consensus between the boards of the Society of Neurology and the Society of Pediatrics for a generally accepted training schedule for childneurology. In 2000, 25 years after the start of the Dutch Society of Child Neurology, an agreement was signed by the two societies. However, child neurology is not a separate subspecialty but a field of interest of both disciplines. This agreement is in accordance with the international discussion and consensus: a neurologist or a pediatrician can be recognised as a childneurologist or neuropediatrician if he/she has been trained during one year in pediatrics or neurology, respectively, and during one year in a recognised centre of child neurology. The performance and interpretation of neurophysiological examinations, particularly electroencephalograms, remain the domain of neurologists in the Netherlands.

The discussion of the relationship 'child neurology versus neuropediatrics' is not restricted to the Netherlands. At the Xth International Congress of Neurology in Barcelona (September 12, 1973), the International Child Neurology Association (ICNA) was established. Ingrid Gamstorp (Sweden) was the first secretary general. Sabine Pelc, a Belgian childneurologist, was responsible for the registration of the articles of the association in accordance with the Belgian law. In her report of the General Meeting of ICNA in Amsterdam (September 17, 1977), Ingrid Gamstorp pointed out that Sabine Pelc was worried by "the dominance of pedriatrics in the training in neuropediatrics in many countries. She fears a majority of not properly neurologically trained members ruling ICNA." In 1979, however, one of the pioneers of the Dutch Child Neurology Society, the neurologist Peek Le Coultre, became president of the ICNA.

Epilogue

In the last decennium, the interest of Dutch pediatricians in child neurology and disabilities associated with pathology of the nervous system has increased. More and more topics, which in the last 25 years have been the domain of child neurologists, have entered the visual fields of pediatricians again. Mental retardation and neurometabolic diseases are diagnosed more and more by pediatricians specialised in clinical genetics or metabolic disorders, respectively. In cases of hydrocephalus, spina bifida, brain tumour, cerebral vascular malformations or focal epilepsy, the neurosurgeon can frequently offer more therapeutic help than the childneurologist whose contribution is largely diagnostic. Rehabilitation of children occurs under the supervision of specialists in rehabilitation medicine. The borders between neurology and psychiatry in infants and children are vague. How the future of child neurology as an interdisciplinary discipline will evolve and to what extent neurologists will continue to contribute to developments remains to be seen. The words of Sabine Pelc still apply.

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Epileptology

13

H. Meinardi

The history of epileptology in the Netherlands has to be seen in an international perspective. In the 19th century several circumstances fertilised the soil on which epileptology was to prosper. In France, Pinel fought against the hospitalisation of people with epilepsy in the hospices for the insane. In the protestant churches a movement arose pleading for the awakening of Christian charity and service to the needy. Effective seizure control was achieved for the first time with the introduction of bromides. The ensuing development of special centres for epilepsy, of which the first in the Netherlands was founded in 1882, has been extensively documented (Meinardi 1972). The definition of epilepsy by Hughlings Jackson as "occasional, sudden, excessive, rapid, and local discharges of the grey matter" was a milestone in the scientific unravelling of the basic mechanisms of seizures. This paper, however, will focus on what happened in the Netherlands or was initiated or promoted by Dutch physicians and scientists. Although epilepsy has been the subject of academic theses in the Netherlands since 1599 (Meinardi 1985), and notwithstanding the fact that in the 19th century Schroeder van der Kolk (1858) published an influential treatise about *The anatomy of the medulla oblongata and its function and about the underlying cause of epilepsy and its rational treatment*, this chapter will focus on the 20th century. On the other hand, actors in the field of epileptology (although hardly historical figures yet) will be reviewed because of their contributions to epileptology in the century selected.

Several approaches to highlight epileptology in the Netherlands are possible. Literature can be searched for publications on epilepsy. Information can be collected about associations or societies that are interested specifically in epilepsy. Furthermore, the achievements of key figures can be put into the limelight. Here a pragmatic mix of these methods is applied. A bird's eye view entails that not all elements that exist in the field of vision can actually be observed. Likewise, this chapter does not pretend to render completely what has happened in the Netherlands to promote knowledge of the various facets of epilepsy and who was responsible. The aim is to offer a sufficient overview of the past in order to get a picture of the development of special centres for epilepsy and the concomitant emergence of epileptology as a science with roots in various disciplines.

The onset of the 20th century

L.J.J. MUSKENS (1872-1937)

L.J.J. Muskens can be rightly called one of the founding fathers of epileptology, and not only because he was probably one of the first Dutch writers to use the term. Muskens and J. Donath from Budapest were secretary of the editorial board and editor-in-chief, respectively, of the journal *Epilepsia*. Together with two physicians not associated with the journal (J. van Deventer, like Muskens from Amsterdam, and A. Marie from Villejuif near Paris) they founded the International League Against Epilepsy (ILAE) (Meinardi 1999).

Muskens became secretary-general of the ILAE and was instrumental in its rebirth in 1935 after World War I had all but wiped it out. A year later he helped to create a federation in the Netherlands, with the aim of pooling all organisations and persons interested in the fight against epilepsy. It was aptly called Federatie voor epilepsiebestrijding (Federation for the Fight Against Epilepsy). At least three quarters of his publications deal with epilepsy. Others testify to different interests in the functioning of the central nervous system, in particular motor coordination and labyrinthine regulation.

Louis Jacob Joseph Muskens was born March 17, 1872 in Mook, a rural town south of Nijmegen. He went to medical school in Utrecht at the age of 17. His thesis on ventricular reflexes in hearts of Rana (frog) summarised his work in Theodor Wilhelm Engelmann's laboratory. Engelmann (1843-1909) was the son-in-law of and successor to the chair of the famous ophthalmologist Frans C. Donders (1818-1891). Cornelius Winkler (1855-1941) decisively influenced Muskens' choice to devote his active years to the study of brain structure and function in health and disease.

Muskens continued his work on cardiac function in the physiology laboratory of Harvard Medical School in Boston, whence he moved to become a resident of Joseph Collins who held the chair of Neurology at the New York Postgraduate Medical School. There he probably had his first exposure to epileptology. Before returning to the Netherlands he worked with Sir William Gowers (1845-1915) and Victor Alexander Haden Horsley (1857-1916) at the National Hospital for Paralytics and Epileptics in London (Eling 2000).

Muskens' paper in the *Nederlandsch Tijdschrift voor Geneeskunde* in 1900 was the opening paper of a series on therapy in psychiatric hospitals. In his paper Muskens emphasises that he will only deal with genuine epilepsy of young people. His experience abroad, in centres with a large number of patients, had provided him with a more optimistic outlook than he expected his readers to have. He warns against indiscriminate use of standard bromide prescriptions as soon as a diagnosis of epilepsy has been made. Furthermore, he emphasises that, as far as possible, the patient and his family are entitled to be informed about prognosis. He was surprised to discover that epilepsy with a hereditary component carries a better prognosis than symptomatic epilepsy. Onset before the age of 30 can have a better prognosis than after that age when epilepsy is usually caused by a cerebral lesion (e.g., a syphilitic infection). Prognosis is better if the type of seizure and the time of the day the seizure occurs is always the same. Successful treatment of grand mal may (at first) increase the occurrence of petit mal (that comprises in this context absence as well as simple partial and complex partial seizures). Crimes may be committed during a petit mal seizure as well as during pre- and postictal confusional states. Convulsions in infancy (according to Muskens, often caused by rickets) predispose to epilepsy. One should abstain from interfering during a seizure. At night a pillow filled with seaweed should be used in order to prevent suffocation during a seizure.

Distinguishing between epileptic and hysteric seizures is difficult. Whereas hysteria is underestimated in children, in adults it is the other way round. It is important to remember that hysterical seizures can start after epilepsy is finally over.

As the central nervous system has the property of use-dependent facilitation of nerve-impulse conduction (in German called 'Bahnung'), the more seizures one has had the more likely epilepsy is to become chronic. Bromide treatment should be titrated to a level at which the patient is constantly a bit dull and sleepy. According to Gowers, so Muskens said, treatment should be continued for three years after the last seizure. According to Feré two years is sufficient. Gowers considered absence of a relapse one year after withdrawal of medication as proof that the epilepsy is cured.

One of the major complications of bromide treatment is acne. Gowers was of the opinion that this can be prevented by the addition of arsenic (12–25 drops of Fowler's solution per day). Where bromide fails or causes intolerable adverse effects borax is the treatment of choice. In cases where the epilepsy resists bromide treatment either borax or zinc can be added (zinc oxide, zinc valerianate, zinc lactate or zinc sulphate). It is also possible to use zinc bromide instead of the usual potassium bromide. It is advisable to record seizures and changes of medication on a calendar. Observing the direction of movement in the tonic phase of seizures helps to diagnose the site of the epileptic focus. From his experience in New York Muskens cites how, according to Hammond, the development of epilepsy may be prevented if children who suffer from convulsions early on in life receive proper care, daily baths, reduction of nitrogenic compounds in the diet (meat, beans), and make a judicious choice of career. There is no objection to marriage.

While the paper quoted appeared under the heading 'Therapy in psychiatric hospitals', Muskens was in fact a prime mover of the establishment of specific hospitals for early treatment of epilepsy as well as residential hospices like those that were established at the end of the 19^{th} and beginning of the 20^{th} century. On his instigation the Nederlandsche Vereeniging tegen vallende ziekte (Dutch Society Against Falling Sickness) was founded in The Hague in 1902. There was a branch of this society in Amsterdam where a building was rented to hospitalise persons with epilepsy. This 'Gasthuis' at the 'Overtoom' initially had A. Bonebakker as medical director and Muskens as specialist for nervous disorders as well as head of the outpatient department. Later the Gasthuis was renamed the 'Alexander van der Leeuw Kliniek', after a patron who had provided a considerable amount of the money required to build a modern hospital in 1920 for people with epilepsy, at the same site as the Gasthuis at the Overtoom in Amsterdam. In 1986, however, it was closed down as part of the restructuring of national healthcare.

Twenty-three years later Muskens published a paper on the history of experimental epilepsy research (Muskens 1923). In it he rejects many publications of famous authors as inept. In his opinion these papers, by Hitzig, Fritsch and Ferrier, Probst, Bubnoff and Heidenhain, and by Unverricht, are of great importance for the understanding of neurophysiology, but do not meet his criteria of relevance for the understanding of epilepsy. The experimental induction of seizures should comply with at least four criteria (Table I).

Table I. Muskens' criteria for true epileptogenic agents.

1. Cause motor activation that occurs at first at very brief intervals and can become continuous. Subsequently, the intervals increase as does the latitude of movement.
2. Not produce systematic contractions, i.e., they should not involve only extensors or only flexors.
3. Be accompanied by totally or partially impaired consciousness.
4. Before and after the actual seizure, pre- and post-epileptic motor, sensory and psychic phenomena should be present.

Muskens believed that seizures experimentally evoked by means of toxic substances was the best way to improve understanding of genuine epilepsy. He states: "Gradually the theory that genuine epilepsy is caused by (auto-) intoxication is most widely accepted and therefore experiments evoking seizures by chemical means are most likely to produce effects comparable to those seen in human epilepsy." After a brief discussion of absinth, picrotoxin, antipyrine, physostigmine and carbolic acid he argues that camphor derivatives are the best tool for investigating epilepsy. He recalls that Purkinje once experimented with an intake of 2.4 grammes of camphor taken in the morning on an empty stomach and had a seizure that, indeed, met the aforementioned four criteria.

Muskens' choice was the compound camphormonobromide. This drug was first introduced as a sedative, apparently without thorough testing, because several reports about its toxicity appeared in the last decade of the 19th century. In rabbits and guinea pigs the hypnotic effect is dominant while in cats and men convulsions are the major symptom. Like other convulsive compounds camphormonobromide reduces body temperature before seizures start. This is interpreted as a defence mechanism. Muskens was surprised that although decrease in body temperature is thought to be a defence mechanism, no suggestion had been made so far that convulsions could be interpreted as a defence mechanism to help eliminate a toxin.

In 1924 Muskens published his *magnum opus: Epilepsie, vergelijkende pathogenese, verschijnselen, behandeling*. In 1926, a German translation was published in the series *Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie*, volume 47. An English edition, *Epilepsy, comparative pathogenesis, symptoms treatment* followed in 1928 with a preface by Sherrington (Courville collection).

The book is divided into three parts:

I History of experimental epilepsy research;
II The effect of interventions in the central nervous system on myoclonic reflexes and myoclonic seizures;
III Epileptic disorders observed in men and their treatment.

While the texts of the first two parts were written in the course of the period 1899-1916 and were reviewed by scientists such as Zwaardemaker (1857-1930) and Magnus (1873-1927), the clinical part, although based on the authors experiences and observations throughout the years 1900-1923, was written without interruption within a much shorter period.

SPECIAL HEALTHCARE PROVISIONS FOR PEOPLE WITH EPILEPSY

Muskens' initiative to start early and adequate treatment of people with epilepsy was put into concrete form at a meeting on January 4, 1902 in The Hague. The meeting was chaired by W.P. Ruijsch (inspector of State Health). Muskens argued that the number of people with epilepsy (PWE) in the Netherlands was estimated to be about 14,000 and that many of them would end up in mental asylums as reflected by a prevalence of approximately seven per cent of PWE in such institutions. He urged the founding of a society to care for the interests of PWE. This society would not be concerned with the care for people with chronic epilepsy as an effective institution for such purpose already existed in the towns of Haarlem/Heemstede. The concern of the envisaged society would be to provide hospital and outpatient care to PWE in the first stage of illness in order to establish a proper diagnosis and provide suitable treatment.

On March 22, 1902 the Nederlandsche Vereeniging tegen vallende ziekte was officially established. As 48 applicant members bought a share for a sum of one hundred guilders in the hospital that was to be founded , and another 252 pledged an annual contribution of two guilders fifty, it was decided to rent a hospital building in Amsterdam. As mentioned above, Bonebakker was appointed medical director and in charge of internal medicine, and Muskens was appointed specialist for mental and nervous diseases and also in charge of the outpatient department. It was intended to open a second outpatient department in The Hague within a short time.

Muskens referred to an existing centre for people with chronic epilepsy in Haarlem/Heemstede. This was the first specialised centre for epilepsy to have been founded in the Netherlands, on January 26, 1882 in Haarlem. The society which was created to make the development of a hospital for people with epilepsy possible, originated as part of the so-called Reveille movement. Well-to-do citizens, who wanted to put their Christian principles into practice, started this movement.

Their reason for starting a special centre for epilepsy was as follows: The owner and director of a Deaconess Hospice in Haarlem, Lady Teding van Berkhout, was approached on several occasions with requests to admit people with epilepsy. These requests were usually rejected and patients were referred to psychiatric hospitals. Finally, two girls were admitted in 1879, but the experiment was a failure. One of the girls had to be taken by coach to Bielefeld, in Germany. The reverend Von Bodelschwingh had started a specialised centre for patients with epilepsy there in 1867. This experience was decisive. With the help of some friends and allies the Christelijke Vereniging voor de verpleging van lijders aan vallende ziekte (Christian Society for the Care of People with Falling Sickness (the Christian Society)) was established and a small building, named Zoar, on Lady Teding van Berkhout's premises was opened for girls with epilepsy, and was partly supported by staff of her Deaconess Hospice.

Initially six girls were admitted, but the pressure for appropriate care for people with epilepsy was such that other buildings soon had to be bought to accommodate an increasing number of patients. All of those buildings bore biblical names, such as the new buildings in Haarlem: Bethesda and Sarepta. In 1885 the mansion Meer en Bosch was acquired as a home for the clergyman-director. A number of buildings were erected around this mansion for patient accommodation and named Salem and Eben Haezer. Because the cradle of the centre, Zoar, no longer existed the name was revived in one of the other buildings on the Meer en Bosch campus. For many years the name Meer en Bosch was used as *pars pro toto* for all activities of the specialised centre, those in Heemstede as well as in Haarlem, and later also for outpatient care centres in various cities.

At first the management was in clerical hands and the medical services were provided by a physician with a practice in the neighbourhood. Soon, however, there was a physician engaged in a more formal relation with the centre. From 1906 to 1927 C.J.C. Burkens held this post. When Burkens suffered a period of prolonged illness, G.C. van Walsem, former professor of medicine in Leiden and former medical superintendent at Meerenberg psychiatric asylum, acted as locum tenens.

Van Walsem stressed the importance of thorough investigation of the PWE in order to advance knowledge about epilepsy and improve the chances for successful treatment. After Burkens' retirement there was a brief interval in which J. van der Spek took over before moving to the post of medical director of the Maasoord psychiatric asylum in Poortugaal near Rotterdam.

In 1930 B.Ch. Ledeboer was appointed as the first medical director alongside the clergyman-director. He was instrumental in creating modern hospital facilities in the centre including an operating theatre. In May 1934 the Koningin Emma Kliniek was opened. In 1955 A.M. Lorentz de Haas succeeded Ledeboer and started to introduce applied research as part of the centre's activities. On his untimely death in 1967 at the age of 56 he was succeeded by a triumvirate: L.M.K. Stoel, clinical director, H. Meinardi, director of research, and H. Wefers Bettink, personnel director. With this change in directorship the office of clergyman-director was abolished.

In 1966, the national regulations regarding the financing of healthcare made it desirable to put the facilities of the Christian Society into separate foundations, named after the major campuses of the institute Meer en Bosch and De Cruquiushoeve. In 1969 these foundations were merged; the new name Instituut voor epilepsiebestrijding (Institute for the Fight Against Epilepsy) was expanded to include Meer en Bosch and De Cruquiushoeve for public relations and fiscal considerations. These two campuses in Heemstede and nearby Vijfhuizen comprise an area of 155 acres.

After the opening in 1966 of the village-like facilities on the former farm De Cruquiushoeve, the Haarlem properties were abandoned. Finally, during the years 1988 to 1992, the political trend of paying more attention to consumer needs resulted in a government decision charging the Instituut voor epilepsiebestrijding to build an annex for 80 patients in Zwolle, for the north-east region of the Netherlands. The special centres for epilepsy were opposed to the creation of new intramural facilities, as modern technological developments had greatly improved diagnosis and monitoring of treatment on an outpatient basis. However, the parents of children with epilepsy, in particular, protested to the Ministry of Health, arguing that when ultimately intramural tertiary care was needed they had no other option but to go to a specialised centre either in the south (vide infra) or the west of the Netherlands.

The order to build a new epilepsy centre was constrained by the demand of the government not to increase the total number of beds in the specialised centres for epilepsy. Therefore, part of the capacity of the centres in Heemstede/Vijfhuizen was transferred to Zwolle, where the new hospital Heemstaete was officially opened on October 8, 1999. This has also resulted in a change of name from Instituut voor epilepsiebestrijding to Stichting Epilepsie Instellingen Nederland (The Society for Dutch Epilepsy Centres) (SEIN). The total number of beds is 680, while outpatient clinics of the SEIN in 10 different towns and cities, covering the Netherlands north of the river Rhine (i.e., Rotterdam [north bank], The Hague, Heemstede, Amsterdam, Alkmaar, Leeuwarden, Groningen, Zwolle, Arnhem and Utrecht) take care of 8,200 outpatients.

After the 80-year war with Roman Catholic Spain, Dutch society became subdivided along religious lines. It is therefore not surprising that, following the successful establishment in 1882 of a Protestant Christian institution, a home for Catholic men with epilepsy was founded. In 1891, Brother Aloysius of the congregation of the Holy Joseph in Heerlen was sent to Wörishofen in Bavaria, Germany to learn about the water cures of Sebastian Anton Kneipp (1821-1897), developed in particular for patients with a weak nervous system. The main reason for his mission was to help the numerous epileptic patients at the Roman Catholic hospices in Heerlen. In 1919, the Brothers of the Holy Joseph in Heerlen decided to start a new foundation in the northern part of the province of Brabant. Brother Aloysius, superior of the congregation, who was caring for epileptic patients in the sanatorium in Heerlen, was one of the delegates who visited the new location, a village called Sterksel, after which the council decided to buy an estate and to build a new house for the care of epileptics.

The first simple convent was opened in 1920 and seven years later a larger building was opened: Huize Providentia. Fifty patients and 13 male nurses moved into the new building. Kwishout, a local physician, provided medical care. A paediatric department was added in 1936. Meanwhile, the first laymen nurses were employed in 1932. During the war, in 1942, the Germans ordered the institute to be cleared. Following the liberation in September 1944 the English used the buildings as a hospital and the institute resumed its original function in 1946.

Kwishout's successor, J.E.H. Rutten, who had become medical director in 1942, was instrumental in re-organising the institute after 1946. In 1953 plans were made to start the first Roman Catholic institute for female epilepsy patients in the Netherlands. The Franciscan congregation was prepared to care for the patients and in 1958 a new foundation was established: Katholieke Stichting voor epileptici in Nederland (Catholic Foundation for Epileptics in the Netherlands). Lorentz de Haas from Meer en Bosch and the neurosurgeon A.C. De Vet from the Ursula Kliniek were members of the medical advisory committee.

In 1962 the construction started of the new centre Kempenhaeghe, located in Heeze near Sterksel, not far from Eindhoven. Two years later the official opening took place. The institutes Providentia and Kempenhaeghe worked closely together, in particular with regards to medical aspects. This resulted in the establishment of a joint foundation called: Stichting medisch centrum (Foundation Medical Centre). In 1970 the collaboration evolved into a complete merger of Providentia, Kempenhaeghe and Foundation Medical Centre into a new corporate body: Stichting Kempenhaeghe. As a consequence there was a redistribution of facilities. Providentia became the unit for the PWE who could not function independently in society.

The epilepsy centre Kempenhaeghe in Heeze has an intramural capacity of 525 beds for inpatients and outpatient departments in four different towns (Enschede, Heeze, Sittard and Maastricht) that care for 3,000 outpatients.

When Kempenhaeghe was initiated, close cooperation with De Klokkenberg foundation in Breda was anticipated. De Klokkenberg is an example how progress in healthcare makes certain provisions redundant and opens opportunities for others. The hospital used to be a large sanatorium for tuberculosis patients. The decreased need for the care of patients with respiratory disorders could no longer justify the continuation of this service. The board of directors obtained permission to compensate for the closure of the sanatorium by establishing departments of epileptology, cardiac surgery, and child psychiatry. Thus, J.H. Bruens, who had successfully defended his Ph.D. thesis on psychotic states in epilepsy at the University of Utrecht in 1963, started a rather small epilepsy centre with 132 beds for inpatients in De Klokkenberg.

In 1965 the epilepsy centre was distinguished from the other units by acquiring the name 'Dr Hans Berger Kliniek'. This centre nowadays also takes care of 2,000 outpatients via clinics in four towns and cities (Breda, Rotterdam [south bank], Goes and Terneuzen). Recently the government decided to close De Klokkenberg; the Dr Hans Berger Kliniek, therefore, is presently discussing a transfer to a general hospital in Breda as the government agreed to maintain the capacity for PWE at the same level.

Several phenomena related to the social forces that determine health provisions can be observed in the development of epilepsy services in the Netherlands. The hospital in Amsterdam, founded at the instigation of Muskens, was located near the Municipal University Hospital. The department of neurology considered this hospital an excellent place to care for chronic neurological patients in general and not just those with epilepsy. Willy-nilly, these referrals were accepted and thus the advantages of a specialised centre for epilepsy were lost.

The Amsterdam epilepsy hospital was closed in 1986. One factor that contributed to its closure was that the costs of building in the centre of Amsterdam made it impossible to expand the building. Accordingly, when specialised centres for epilepsy began to engage in rehabilitation and provide sheltered workshops for their patients, Amsterdam had to default.

Earlier in this chapter the social compulsion for the Instituut voor epilepsiebestrijding to build an annex in Zwolle was mentioned. The closure of De Klokkenberg was also politically motivated. First, a conflict within the management of the unit for cardiology and cardiac surgery could not be resolved and the government decided that this unit should be closed. Consequently, this has resulted in a decision to place the remaining units (epilepsy, respiratory diseases and child psychiatry) next to or attached to general hospitals or other services in the same field, such as the municipal mental health facilities. It is too early to gauge the impact that this measure will have on tertiary care for PWE.

Epileptology before and shortly after World War II

Muskens' contribution to the development of epileptology in the Netherlands has already been mentioned. Maybe one of the most important feats has been his emphasis on the need for special centres. These have become an important source for the further development of epileptology.

Exploring the past often reveals a mixture of antiquated and obsolete as well as logical and astute observations that have stood the wear and tear of time. For historical reasons some of the papers that concerned dead-ends will nevertheless be mentioned. For example, as Muskens mentioned, when defending his choice of camphormonobromide as the best tool to study epilepsy, the theory that genuine epilepsy is caused by (auto-)intoxication was en vogue at the onset of the 20th century.

G.C. BOLTEN (1872-1940)

G.C. Bolten was neuropsychiatrist in The Hague and he had a great interest in epilepsy. Nevertheless, as far as can be verified he never became a member of any of the organisations that were founded in order to improve care and treatment of PWE. He was a proponent of the auto-intoxication theory. In 1913 he published a treatise on pathogenesis and the treatment of 'genuine' epilepsy. Bolten opposed the theory of pathologic changes of brain tissue as a cause of epilepsy for two reasons: first, the two most characteristic abnormalities in the brain, i.e., ammonshorn sclerosis and marginal gliosis are only seen in chronic cases; second, these pathological changes are not specific to epilepsy as they also occur in various psychoses that are accompanied by dementia.

In his opinion the theory of chronic auto-intoxication was much more convincing. He pointed out the fact that there are many toxins that cause seizures albeit different from those of epilepsy. The differences can be explained by the toxin. As the cause of epilepsy he postulated that there is an endogenous substance that is adequately detoxified and removed in most people. This mechanism fails in epilepsy, and seizures are an unpleasant and sometimes dangerous natural defence mechanism of the body to get rid of the gradually increasing levels of auto-toxin. In a series of experiments Bolten administered consecutively pressed juice of about all the endocrine glands by rectal route. While none of the juices caused any exacerbation of seizure frequency, the combined administration of thyroid and parathyroid juice had a considerable effect on those with genuine epilepsy. In some cases seizures stopped almost immediately, in others it took longer, occasionally even six to eight months. However, in all cases, provided secondary dementia had not yet occurred, there was a great improvement. In a paper published less than a year later he offered an explanation why genuine and cortical epilepsy look so similar (Bolten 1914). In both cases he postulated a gradual accumulation of toxins in the cerebral cells. In the case of genuine epilepsy it is a toxin produced outside the brain because of thyroid/parathyroid insufficiency; in the case of cerebral (cortical) epilepsy pathological changes of the brain impair vascular drainage of toxins produced by cerebral activity. Seizures are interpreted as a defence mechanism that eliminates the accumulated toxins. This explains why many people with epilepsy feel much better after a seizure.

J.J.H.M. KLESSENS (1888-1972)

J.J.H.M. Klessens, who, as medical director, was in charge of the special hospital for PWE in Amsterdam from 1918, published 15 years after Bolten: *Some considerations about the essence and the origin of epilepsy* (Klessens 1928). He observed that most authors agreed that epilepsy could not be considered a primary disorder of the brain. The brain serves as vehicle to produce the symptoms of epilepsy but epilepsy itself is not localised in that organ. He also refuted the concept that epilepsy is hereditary as his own studies of 750 persons with epilepsy yielded that less than eight per cent of those studied had a relative who also suffered from epilepsy.

Klessens expected a theoretical basis for the origin of epilepsy to come from a theory developed by Von Kraus about the autonomic/endocrine/vegetative system of the body. This explanation, according to Klessens, opened a whole new approach to the treatment of epilepsy. While thus far only the symptoms (i.e., the seizures) had been treated by sedatives (bromides, phenobarbitone, borax), now prophylactic therapies could be developed by removing the patient from a pathogenic environment (by hospitalisation) or by influencing the vegetative nervous system and hormone production. His point of view about an external (non-brain related) origin of genuine epilepsy was maintained in one of his last contributions about epilepsy in a Dutch medical journal entitled *Sexual function and epilepsy* (Klessens 1948). His closing remark in that paper is: “Changes in the electroencephalogram between the fits need not compel us to accept the assumption that the primary cause of epilepsy is situated in the brain."

B.C. LEDEBOER (1897–1959)

Notwithstanding Klessens' statement that genuine epilepsy was generally accepted not to be a primary brain disorder, Ledeboer, the medical director of the special centre for epilepsy in Haarlem/Heemstede, could not be counted among the believers. His firm opinions are clearly stated in a survey of the epilepsies written at the end of his career (Ledeboer 1953). In contrast with Klessens, he refers to the epilepsies as intrinsic brain disorders due to endogenic and exogenic factors. Although he admits that evidence of a hereditary factor is only demonstrable in a small percentage he argues that genetic factors do play a role where exogenic factors cannot be found. Ledeboer also considered alcoholism to be an endogenic factor. To his surprise, psychic trauma, in particular extreme fear, to which some people were exposed during World War II, appeared to be an important exogenic factor. He distinguishes four therapeutic approaches, although he points out that, occasionally, abstinence of therapeutic interventions may be of greater benefit to the patient and has always to be taken into consideration. Pharmacotherapy is indicated in the first place, a ketogenic diet may prove beneficial in children up to 14 years, neurosurgery is an option, and psychosocial therapy is indicated usually as adjunctive and occasionally as primary intervention. He emphasizes that most types of jobs are possible once the seizures have remitted completely, but if seizures persist, he proffers a list of possible occupations. He cautions that withdrawal of medication after remittance risks relapse and in such cases it may be difficult and sometimes impossible to regain seizure control.

Under his leadership the centre for epilepsy in Heemstede/Haarlem evolved from a residential care centre to a comprehensive centre that included hospital facilities, a neurosurgical theatre, a special school for children with epilepsy, rehabilitation services and a network of outpatient clinics across the Netherlands. Shortly after World War II (1946) he was, as Muskens before him and several other Dutch epileptologists after him, appointed a member of the Executive Committee of the ILAE. He served first as vice-president and then as secretary-general until 1957 (Meinardi 1999).

Soon after his appointment as medical director in 1930, he introduced the ketogenic diet (De Wilde-Ockeloen 2000). Ledeboer also made early use of cinematography both for the recording of seizures and for public education as well as for fundraising. Before World War II there had been one Dutch publication on the use of electroencephalography for epilepsy using an electrocardiograph with a especially constructed pre-amplifier (van der Molen 1939), but Ledeboer is credited with installing the first Grass EEG-machine in the Netherlands for regular use in diagnosis and monitoring of epilepsy in Heemstede in 1947.

Ledeboer's organisational talents stood him in good stead when the Germans occupied the Netherlands and tried to impose their rules and policies about eradication of presumed hereditary disorders on the centre. When the occupying power replaced the governors and the director, a well-prepared plan was executed to transfer all in-patients either to their homes or to other hospitals under other diagnostic labels. Two outpatient clinics, of the ten that would later form a network scattered over the Netherlands north of the Rhine, had already been established in Apeldoorn (1934) and Leeuwarden (1937). The staff of these clinics formed an important force in the support of the patients in hiding.

Before further reviewing what happened to epileptology after World War II, work should be mentioned of two Dutch authors who, in the pre-World War II period, made original contributions to the field, one still remembered in an eponym, the other long forgotten.

E. WIERSMA (1858-1940)

E. Wiersma was interested in the significance that has to be attributed to frequency and duration of changes in the threshold of observation (Wiersma 1909). Accordingly he became interested in epilepsy. He reasoned that most pathological states can be considered deviations from normal physiological functions. A primary dysfunction will cause a cascade of interrelated disturbances. It is essential to identify the primary dysfunction, as full-blown illness will present a pattern that is difficult to analyse.

Wiersma argued that correlation of seizure onset with falling asleep and, furthermore, auras of *déjà vu* and *jamais vu* (in his words expressions of depersonalisation and false recognition) indicated a primary dysfunction of the normal fluctuation in perception threshold. In the course of these studies he developed a test for vigilance still very much in use although no longer believed to be pathognomonic for epilepsy. As this test is similar to a test introduced by J.B.I. Bourdon (1796-1861), a physician in Paris, it is known as the Bourdon-Wiersma test.

J.C.L. GODEFROY

Godefroy was one of Wiersma's Ph.D. students in Groningen and thus became involved in studies of epilepsy. His object of analysis was the slowing of the motor function. He remarks that people with epilepsy are considered accurate and exact workmen. However, although qualitatively their work comes up to the requirements, quality is only maintained at the expense of a disproportionate decrease in quantity.

Several tests existed that try to register and assess the actions of persons with epilepsy, but very slight disturbances were often not shown in the final result. Godefroy (1921) tried to find a method that allowed recognition of the effect on movement of the slightest lapse of consciousness. He found this in the work of Gillbrett, who analysed the greater or lesser productivity of a factory hand by attaching a small incandescent lamp to the moving part of the body. The movement was thus recorded as a thin light line on a photographic plate. Although the method is elegant there is little or no reference to it in the literature.

Epileptology after World War II until the end of the 20th century

THE SPECIAL CENTRE FOR EPILEPSY IN HEEMSTEDE/HAARLEM/VIJFHUIZEN

W. Kramer (1915-)

About a year after Ledeboer's survey , one of his co-workers, W. Kramer, who was in charge of the female ward, published (Kramer 1954) an analysis of 272 women, aged 8-60 years, whose epilepsy had been investigated in the hospital part of the centre.

Notwithstanding systematic use of cinematographic recording of seizures, Kramer found this tool of little help in distinguishing categories of seizures. Results of therapy are expressed as: seizure free; 75, 50, 25 per cent reduction of frequency; or no benefit. Kramer pointed out that the quality of life for some patients was better if suppression of seizures was not rigidly pursued.

His attempt to classify seizures bears a certain resemblance to the classification of seizures by the ILAE. However, the work on this latter classification started ten years later at the first meeting of the Commission on Terminology and Classification of the ILAE. By coincidence this meeting took place in the same centre, however, by that time Ledeboer and Kramer had both left and Lorentz de Haas had become the centre's medical director.

Attempting to correlate findings of the study with presumed causes Kramer notes that these endeavours are frustrated by the fact that one and the same cause may give rise to different pathology depending on the age at which it acts on the brain. On the other hand various causes may produce similar pathological alterations if they hit the brain at the same time of maturation.

Despite the laborious work presented, the author concluded that with the knowledge available it was impossible to classify epileptic syndromes.

A.M. Lorentz de Haas (1911-1967)

Albert M. Lorentz de Haas was the son of De Haas, professor of physics in Leiden and grandson of the Nobel laureate Lorentz, whose name was added to his father's name as Lorentz did not have any male descendants. He was invited in 1951 to take over from Klessens as medical director of the Alexander van der Leeuw Kliniek. Before doing so he was allowed to take further training in epileptology with William Lennox and Jerome Merlis in Boston. His period in charge of the Alexander van der Leeuw Kliniek was short-lived as Ledeboer's position as medical director of the much larger and multifaceted special centre for epilepsy in Heemstede/Haarlem, became vacant and was offered to Lorentz de Haas, who accepted the post in 1955.

One of the steps forward introduced by Lorentz de Haas was an improvement in the rehabilitation of people with epilepsy through the establishment in this special centre of the first and only governmental sheltered workshop specifically for people handicapped with epilepsy.

Given his background he had an open eye for the need for research in a special centre for epilepsy. In 1961 Lorentz de Haas invited G.W.F. (Boy) Edgar, an accomplished neuroscientist, and in his leisure time leader of a world famous jazz-band, to develop a research laboratory at the Meer en Bosch campus. Furthermore, he agreed to offer Meinardi a post for both clinical and research work after the latter's return from the United States of America. Lorentz de Haas continued the tradition of Dutch participation in the leadership of the International League Against Epilepsy, first as vice-president (1961-1965) and subsequently as president (1965-1967), this period being cut short by his untimely death in 1967. During both periods Lorentz de Haas was co-editor of *Epilepsia* with Henri Gastaut (from France). The journal of the Netherlands Society of Psychiatry and Neurology also availed itself of Lorentz de Haas's talents and elected him first as editor (1950-1958) and next as editor-in-chief (1958–1967) of their journal *Folia Psychiatrica, Neurologica et Neurochirurgica Neerlandica*.

As a part of the modernisation of the special centre for epilepsy in Haarlem/Heemstede, Lorentz de Haas closed the nursing home type accommodation for those people with epilepsy who would never be able to look after themselves, in particular because of the combination of epilepsy and associated handicaps. Instead a village type accommodation was built in Vijfhuizen, about three kilometres from the Meer en Bosch campus in Heemstede. This residential care centre was named De Cruquiushoeve after the farm on whose land it was established (Lorentz de Haas 1967).

When Lorentz de Haas took over from Ledeboer he also closed the operating theatre as, in his opinion, it was safer for the patients to be operated upon at the Ursula Kliniek in Wassenaar, about 30 kilometres south of Heemstede, where operations for all kinds of neurological disorders took place, thus assuring the availability of highly experienced staff.

O. Magnus (1913-)

Otto Magnus would have been Lorentz de Haas's successor par excellence. However, the board of governors of the special centre for epilepsy Meer en Bosch/De Cruquiushoeve decided to split the medical directorship between a clinical and a research director. This concept of a board of directors was becoming in vogue but clashed with the principle of 'one captain, one ship' and Magnus declined to be part of such a management team. Nevertheless, thanks to Otto Magnus temporarily taking over Lorentz de Haas's commitments, the gap caused by Lorentz de Haas's death was bridged without too many calamities. Amongst other commitments, he stood in as editor-in-chief of *Epilepsia* until, at the next election of ILAE executive committee members, he was elected secretary-general and the post of editor-in-chief went to Margaret Lennox-Buchthal.

Magnus had in fact been associated with the special centre for epilepsy since 1950 as head of the EEG-laboratory. His interest in clinical neurophysiology dated from World War II. Magnus (on the run from the German invasion of the Netherlands) was able to reach Switzerland and obtained a position in the laboratory of professor W.R. Hess.

After the war he was offered an appointment as clinical electro-encephalographer in order to support, among other things, the neurosurgery performed by A.C. de Vet (1904-2001). Before embarking on pre-, per-, and post-surgical electroencephalography Magnus spent a year at the Montreal Neurological Institute with Penfield and Jaspers. De Vet was the first neurosurgeon at the Ursula Kliniek in Wassenaar as well as being neurosurgeon in attendance in the special centre for epilepsy until around 1955 when Lorentz de Haas decided that all operations should be carried out in Wassenaar itself. While the neurosurgery moved to Wassenaar, the electroencephalography remained in Heemstede and Magnus was in charge of that department up to 1968 when Anneke Kuyer took over.

In 1971 Magnus and the *hic tempore* general-secretary Mia Slag of the Health Organisation for Applied Research (GO-TNO) conceived a way to improve funding of epilepsy research. Advice about grant applications and also about policies to promote research in the field of epilepsy was to be provided by an independent committee of GO-TNO called CLEO (Commission for National Epilepsy Research). Meinardi became its first 'coordinator'. This commission was quite effective in stimulating and supporting epilepsy research in the Netherlands. In 1993 it was transferred to the Nationaal Epilepsiefonds (National Epilepsy Fund) where it continues to function albeit under a slightly different name (Wetenschappelijke adviesraad Nationaal epilepsiefonds; Scientific Advisory Board National Epilepsy Fund).

H. Meinardi (1932-)

H. Meinardi became interested in epileptology in 1954 while working as a student in the endocrinology laboratory of A. Querido in Leiden. In 1960 he defended a Ph.D. thesis on the action of hydroxydione on the peripheral nerve, intended to be a step in elucidating the role of hormones in catamenial epilepsy. In 1962 he was accepted at the postgraduate school of the Rockefeller Institute. Four years later, although he had not yet finished these studies, Lorentz de Haas asked him to return to the Netherlands if he was still interested in a combined appointment in the new research laboratory and in clinical work at the special centre for epilepsy. This he did.

When Lorentz de Haas died and Magnus disagreed with the concept of a board of equipotent directors, the board of governors appointed Lambertus M.K. Stoel, Harry Meinardi and Henk Wefers Bettink as clinical director, director of research and director of personnel, respectively.

From the board of governors Meinardi obtained the commitment that academic staff were allowed to spend ten per cent of their time on research either in between other duties or *en bloc*. Furthermore, the health insurance companies agreed that the status of a special centre for epilepsy demanded finances to advance knowledge about the disorder and its consequences. Thus several collaborators were able to devote sufficient time to research to fulfil the requirements of a Ph.D. degree (Smits 1970, Voskuyl 1978, Kuyer 1978, van Zijl 1979, Overweg 1985, Kasteleijn-Nolst Trenité 1989, and Meijer 1991). Furthermore, staff of the Instituut voor epilepsiebestrijding assisted several extraneous Ph.D. students whose research required the facilities and patients of the special centre (Spaans 1971, Suurmeijer 1980, and Lindhout 1985).

From the chairman of the department of physiology in Leiden (professor J.W. Duyff) Meinardi received facilities to perform experimental studies on epilepsy. This unit is presently managed by R.A. Voskuyl. Initially focused on understanding epileptogenesis by analysis of the action of penicillin, the experimental work later supported the search to understand the action of antiepileptic drugs.

At the centre in Heemstede itself the bulk of research concerned various aspects of antiepileptic drug treatment. The first double blind cross-over trial of a new antiepileptic drug, sodium valproate, was performed in Heemstede thanks to collaboration with F. A. Nelemans and W.G. Zelvelder of TNO (Meinardi 1971).

The fact that J.W.A. Meijer, a brilliant chemist from Leiden who had been pioneering in gas-chromatography, joined the research team in Heemstede has been responsible for much of the progress achieved. The work in Heemstede became integrated in an international network through a series of WODADIBOFs (Workshops on the determination of antiepileptic drugs in body fluids: Meijer 1973, Schneider 1975, Gardner-Thorpe 1977, Johannessen 1979). The same concept was later used to thrash out other problems in epileptology (Kulig 1980, Oxley 1983, Martins da Silva 1985, Frey 1986, Aldenkamp 1987, Dreyfuss 1990, Meinardi 1993).

When it became clear that it would no longer be possible to combine the registrations of neurology and psychiatry (notwithstanding protests by J.J.G. Prick and Meinardi, among others) Meinardi, who by that time had become general director of the Instituut voor epilepsiebestrijding, decided to put neurologists together with psychologists in multidisciplinary teams that served the patients of the special centre. Like all academic staff only part of their duty was to engage in research. Nevertheless, several important contributions were made; in particular professor A.P. Aldenkamp has become an internationally recognised leader in the field.

C. Binnie (1938-)

Colin Binnie joined the Instituut voor epilepsiebestrijding in 1976 to take charge of the EEG-department. He brought with him a Cambridge Electronic Design Alpha-2 computer and a strong interest in pattern and flash induced responses in people with epilepsy.

Furthermore, Binnie developed a technique for cable telemetry and was a key person in the development of pre-surgical evaluation of people with epilepsy. Binnie returned to the UK in 1985 as the possibility to obtain a part-time professorship in clinical neurophysiology in Utrecht was blocked because he was not a registered neurologist. His post in Heemstede was taken over by W. van Emde Boas who consolidated and further expanded the collaboration of the Instituut voor epilepsiebestrijding with the department of neurosurgery of the Utrecht University Hospital (professor C.W.M. van Veelen) to form the epilepsy surgery unit for the Netherlands.

THE SPECIAL CENTRES FOR EPILEPSY IN HEEZE/STERKSEL AND BREDA

The financial conditions to enable research were much less favourable in the two southern special centres. Nevertheless, in Kempenhaeghe, J.A.R.J. Hulsman and Th.W. Rentmeester, head of the clinical chemistry department and clinical neurologist, respectively, played a pivotal role in ensuring that at least research of international standard about efficacy and tolerability of new antiepileptic drugs could be conducted. A.C. Declerck, head of the EEG-department in Kempenhaeghe, because of his interest in sleep and epilepsy, developed a sleep-research centre also dealing with non-epilepsy related sleep pathology. This work, however, is outside the context of the present chapter.

A.E.H. Sonnen (1931-2000)

The expectation had been (given the interest of its founder J. Bruens in psychiatry) that the Dr Hans Berger Kliniek in Breda would specialise in the association of epilepsy and psychiatric symptoms. Although this interest was reflected in the referrals of patients who were difficult to treat, no specific research in that field emanated from this institute. The scientifically most prolific of the staff-members, although he never bothered to use his talents for the acquisition of a formal Ph.D. degree, was A.E.H. Sonnen. His work, in particular about risk assessment, contributed to the formulation of European guidelines for the issuing of driver's licences. As the Dr Hans Berger Kliniek was part of De Klokkenberg hospital, which included a centre for cardiac surgery, Sonnen was also in the position to perform the first Dutch evaluation study of vagus nerve stimulation in the management of epilepsy.

UNIVERSITY BASED EPILEPSY RESEARCH

As the chronic character of epilepsy is in conflict with the teaching requirements of university hospitals, which results in frequently changing staff on the wards and in the outpatient clinics, the need for tertiary epilepsy centres was clear. This kept problems associated with epilepsy somewhat outside the scope of universities, until the development of child-neurology departments changed this to some degree. Nevertheless, the University of Nijmegen did have a tradition in epilepsy research. Professor O. Hommes pursued the analysis of the relationship between folic acid and seizures for many years, and E. van der Kleyn, head of the department of pharmacy, markedly contributed to insight in the pharmacokinetics of antiepileptic drugs, while G. van Luytelaar initiated the use of the Wag/Rij rats suffering from absence seizures as model for further elucidation of various problems in epileptology. The University of Nijmegen interdisciplinary paediatric/neurological department for child-neurology had been the first to appoint a staff member as lecturer in epileptology, i.e., W.O. Renier. This tradition may have contributed to the fact that Nijmegen University was the only one of the six Dutch universities to have accepted an endowed chair for epilepsy, in 1984, although even there it had to be called a 'professorship in the science of fighting epilepsy' (Meinardi 1985). W.O. Renier recently took over from Meinardi; on this occasion the title was changed into professor of epileptology and the status of the chair became more imbedded in the organisation of the University.

The obvious interest of child-neurologists in epilepsy has resulted in the Netherlands in the concerted South Netherlands Child Epilepsy Research with key-figures W.F.M. Arts, A.C.B. Peters and C. van Donselaar. The latter has recently been appointed on an endowed chair of Epileptology at the University of Utrecht.

Storm van Leeuwen (1912-) and Lopes da Silva (1935-)

Some of those who made important contributions to epileptology in the 20th century did so at an advanced stage of their career. Storm van Leeuwen initiated the department of electroencephalography at Leiden University. Later he moved to become head of the Institute for Medical Physics of the Health Organisation for Applied Research in Utrecht and was appointed to the chair of Clinical Neurophysiology at Utrecht University. In the latter capacity he started the Dutch Working Group for Neurophysiological Surgery. This group initially dealt with the assessment and surgery of both psychiatric and epileptic patients. Later its focus became more or less restricted to epilepsy surgery.

A brilliant Portuguese neurologist, F. Lopes da Silva, who had emigrated to the Netherlands, worked at the Institute for Medical Physics Through the work on epilepsy surgery he became involved in the epilepsy field, that suited his general interest in the functioning of brain and mind. At the time that Meinardi retired from the Instituut voor epilepsiebestrijding, Lopes da Silva combined the reactivated post of director of research in Heemstede with the chair of professor in General Animal Physiology at the Faculty of Sciences at the University of Amsterdam. He still held these posts at the end of the 20th century, where this overview ends.

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Neuromuscular Diseases

14

F.G.I. Jennekens

In the history of research of nerve and muscle diseases, the second half of the nineteenth century was an exceptionally fruitful period. Many of the most frequent diseases of these tissues were discovered in this period, predominantly by clinicians in France, Germany and England. Dutch research contributed little at that time, with one striking exception. This concerned a health problem in one of its colonies. Beriberi had already been known for more than a 1000 years (Bergsma 1917). In the second half of the 19th century, it caused the death of many soldiers and sailors in and near Atjeh, in the northern part of Sumatra, where freedom-loving people were living. The Dutch government wanted to put an end to these losses and sent two medical scientists, Cornelis A. Pekelharing (1848-1922) and Cornelis Winkler (1855-1941), on a fact-finding mission. In 1888, these authors provided the medical world with a "comprehensive and lucid" report of the clinical features and a "detailed description" of the pathological changes of the peripheral nerves, based on "surprisingly modern methods of examination" (Victor 1984). The patients studied showed symptoms and signs of what the authors described as 'névrite périphérique multiple' [multiple peripheral neuritis] and cardiac failure (Winkler and Pekelharing 1918). The 'neuritis' was due to axonal degeneration of peripheral nerves, which was much more severe in the periphery than proximal. Beautiful drawings of isolated nerve fibres showed remyelination and myelin ovoids (see Fig. 1).

Figure 1.
Drawings by Winkler and Pekelharing of osmicated, teased nerve fibres from patients with beriberi, showing myelin degeneration secondary to axonal degeneration and remyelination (figures 3, 4, 6, 9, 10 and 11 from plate V, in 'Winkler en collaboration avec Pekelharing' 1918).

Unfortunately, while the condition was now well mapped out, the cause remained a mystery and the goals of prevention and treatment were still as distant as before. Christiaan Eijkman (1858-1930), who had assisted in the investigations of Pekelharing and Winkler, aimed to change this. He was a pathologist with experience in infectious diseases and had been appointed director of the Research Laboratory for Pathological Anatomy and Bacteriology in Batavia (now Djakarta). He succeeded in producing beriberi in chicken and concluded in 1896 that the disease was caused both in animals and humans, by a diet of polished (over-milled) rice. His successor, Gerrit Grijns (1865-1944) suggested that beriberi was a deficiency disease instead of a toxicological disorder, as Eijkman believed (Morton 1983). In 1929, Eijkman received the Nobel Prize for his discovery.

At present, neuromuscular diseases are considered to comprise diseases of the skeletal musculature and the peripheral nervous system including the lower motor neurones. This makes beriberi a neuromuscular disease. The discovery of polished rice as a cause for beriberi has become part of the 'prehistory' of Dutch neuromuscular research.

State-of-the-art halfway through the last century

In 1953, Arie Biemond (1902-1973) published his monograph on 'Disorders of the Spinal Cord and Peripheral Nerves' thereby earning himself a permanent place in the history of neuromuscular diseases in the Netherlands. The value of his book for readers of today lies in the fact that it summarises the knowledge about diseases of nerves and muscles in the Netherlands half a century ago. It marked the end of the pre-neuromuscular period in the history of Dutch neurology. Electromyography was still in its infancy and modern methods of histochemistry and electronmicroscopy had not yet been incorporated in the diagnostic methods. Most clinicians were not yet aware of the significance of modes of inheritance for diagnosis, prognosis and prevention of hereditary diseases.

Table I. Nerve and muscle diseases according to A. Biemond (1953).

Diseases of lower motor neurones	Diseases of nerves	Diseases of muscle
1 Poliomyelitis	1 Peripheral nerve lesions	1 Progressive muscular dystrophy
2 Amyotrophic lateral sclerosis	2 Polyneuritis	2 Myositis and polymyositis
3 Progressive spinal musc. atrophy	3 Plexus brachialis disorders	3 Myasthenia
4 Infantile spinal musc. atrophy	4 Neurogenic muscular atrophy	4 Myotonia
	5 Nerve tumours	5 Periodic paralysis
	6 Neuralgia	6 Crampi musculorum
	7 Tetany	
	8 Tetanus infection	

Abbrevation: musc. =musculature

Biemond distinguished four diseases of the lower motor neurones, eight disorders or categories of disorders of peripheral nerve diseases and six categories of muscle diseases (Table I). The main clinical features of amyotrophic lateral sclerosis (ALS) were well known. Poliomyelitis anterior chronica, also called spinal muscular atrophy, was, according to Biemond, occasionally reversible or relapsing! The mode of inheritance of Werdnig-Hoffmann disease was not mentioned and other types of autosomal recessive spinal muscular atrophy had not yet been discovered. Among the peripheral nerve diseases, he classified tetany and tetanus infection. Tetany at the time was probably much more of a problem than it is nowadays, as assessment of serum electrolytes had not yet become a routine. Tetanus infection causes really dysfunction of lower motor neurones and was apparently of practical significance for Dutch neurologists. These days, this infection is not usually included in textbooks on neuromuscular diseases. The clinical features of the carpal tunnel syndrome were well known and were thought to be caused by a plexus brachialis disorder. Charcot-Marie-Tooth and Dejerine-Sottas polyneuropathies remained hidden under the heading of neurogenic muscular atrophy.

Biemond's list of muscle diseases comprised six categories. In the muscular dystrophies, limb girdle dystrophy was distinguished from facioscapulohumeral muscular dystrophy, while infantile pseudohypertrophic dystrophy, designated as Duchenne-Friedreich's muscular dystrophy was separated from other limb girdle muscular dystrophies. Apparently, Biemond had no experience with the congenital and ocular muscular dystrophies nor with distal myopathies and therefore these were not mentioned. He was aware of three myotonic diseases (myotonic dystrophy, myotonia congenita and paramyotonia) and of periodic paralysis. He himself had been one of the first to recognise the association of this latter disease with hypokalaemia (Biemond and Polak Daniels 1934). Pompe's disease was not included in the list of muscle diseases despite the fact that the pathology of this disorder had been described for the first time by a Dutch pathologist at a meeting in Amsterdam (Pompe 1932).

Almost 50 years after Biemond's book had come on to the market, a handbook on neuromuscular diseases was published by Marianne de Visser, Marinus Vermeulen and John H.J. Wokke (1999). It contained descriptions of approximately one hundred disorders or categories of disorders of nerves and muscles and illustrated the stunning explosion in knowledge in the second half of the 20th century, comparable only – though not similar – to what had happened to neurology in the second half of the 19th century. Dutch physicians had contributed to this increase of knowledge and had made sure that patients benefited from the scientific advancements.

In the following, I shall first describe the onset of research of neuromuscular diseases and the effects for patients with these diseases and how it spread over all large medical centres in the country. The second part deals with the role of the Dutch society for patients with neuromuscular diseases and the funding of Dutch neuromuscular research. The final part is devoted to recent developments.

Research and care

A PIONEER

Figure 2.
Joop G.Y. de Jong was a pioneer in Dutch neuromuscular research and described in 1947 hereditary pressure palsy.

The map of the Netherlands shows, in the south-east, a trunk which gradually broadens into a bag. This bag is the southern part of the province of Limburg, which is bordered on three sides by Belgium and Germany. It is densely populated and has four major towns, the largest and oldest being Maastricht. During and after the Second World War, neurological and psychiatric care in this southern part of Limburg was provided by three nerve specialists. Joop G.Y. de Jong (1909-1998) was one of them. He had his base in Heerlen, the centre of a mining district with 50.000 inhabitants, which was at that time approximately 160 kilometres from the nearest Dutch university department of neurology. He was a short and stout man, an orthodox and pious Roman Catholic with an affinity for the arts (Fig. 2). He wrote songs for his nine children and sang them, together with his family, at his children's birthdays. He had a huge practice and a great interest in hereditary disorders. He discovered a disease that occurred in three generations of one family; the family concerned called it 'potato-dig-up disease'. The name referred to the transient peroneal weakness that arose during harvest-time when the family members had to collect potatoes. De Jong's observation of the disease led to the first publication on hereditary pressure palsy in 1947, in the journal of the Netherlands Society of Psychiatry and Neurology. Biemond made no mention of hereditary pressure palsy in his book and, though there was no lack of patients, it took 18 years before another Dutch article on hereditary pressure palsy was published. Undismayed, de Jong went on with an extensive study on myotonic dystrophy and published eleven large pedigrees of families with this disease in a comprehensive doctorate thesis on myotonia (1955). He was one of the first authors to recognise the age-of-onset related psychopathological differences in myotonic dystrophy. De Jong was neither a leader nor a trendsetter; rather he was a forerunner. He never had any followers and scarcely any admirers. However, forty years later his data were used in the first extensive study on survival of patients with myotonic dystrophy (de Die-Smulders et al. 1998).

THE FOUNDER

Jaap Bethlem was a slim, rather tall and elegant man with great attention for detail and a tendency to dominate (Fig. 3). In contrast to de Jong, his clinical and research activities were within a very limited field. He specialised in neurology in Biemond's department in the early 1950s and was sent to Queen Square for a one-year training period in neuropathology where he had the opportunity to perform microscopy on autopsy material from two patients with myotonic dystrophy. Once he had returned to Amsterdam, he performed a study of myotonic dystrophy pedigrees and, ignorant as he was of de Jong's work in another part of the country, he wrote his doctorate thesis on this disease. He published and defended this thesis in Amsterdam in 1955, almost simultaneously with de Jong's defence of his thesis on myotonia in Utrecht. It was a carefully written, succinct and thin book with much attention for myopathology. He was given the responsibility for the neuropathology laboratory in Biemond's department and while fulfilling his obligations of studying the whole nervous system and publishing about central nervous system abnormalities, he maintained a keen interest in the skeletal musculature.

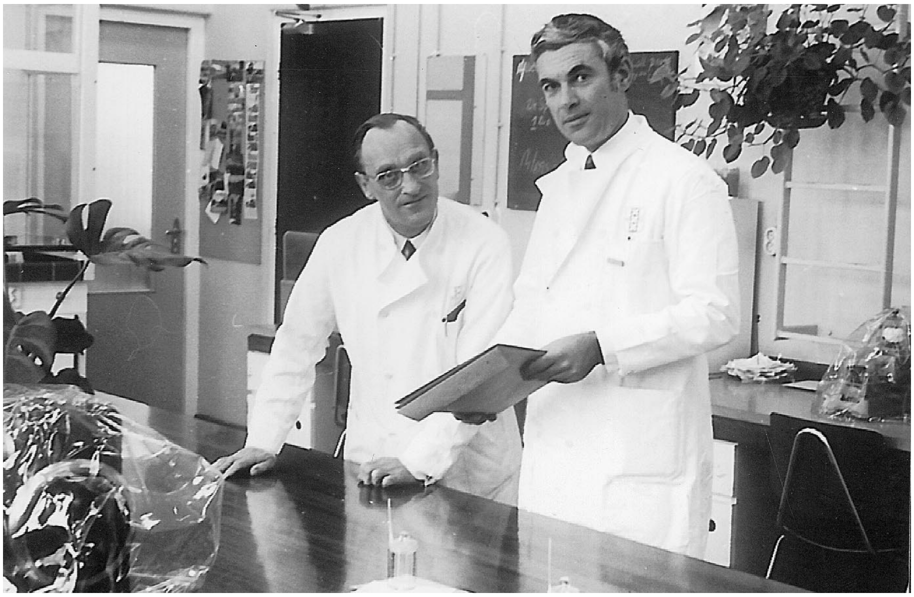

Figure 3.
Jaap Bethlem, the founder of Dutch neuromuscular research, at the age of approximately 48 years. The picture has been taken in the neuropathology laboratory of the department of neurology of the University of Amsterdam. Standing beside him is Arie Westerveld, the chief technician of the laboratory.

In the sixties, when new techniques revolutionised the methods of investigation of patients with myopathies, Bethlem succeeded in bringing together several different specialists to diagnose patients with unknown skeletal muscle diseases. A young clinician, George K. van Wijngaarden, carried out the neurological examinations of new patients at the outpatient department, one surgeon took all muscle biopsies while the biochemist Hugo E.F.H. Meyer in the pathology laboratory accepted responsibility for the histochemical techniques in 1965. Bethlem was the neuropathologist and coordinator and posed the final diagnosis. Patients came from all over the country to this outpatient clinic and underwent a series of examinations in one day. They returned home in the afternoon and after a few weeks or months a description of the main findings, the diagnosis and advice were sent to the referring physician. It was not customary to see patients a second time because it was felt that treatment was not usually possible. The Centre for Myopathies, as Bethlem called it, became a great success due to the patients that were referred and the opportunity they offered for research. In a series of outstanding articles, he and van Wijngaarden and their collaborators contributed to the rapidly growing knowledge of rare congenital and hereditary myopathies with original case studies and studies on pedigrees. One of Bethlem and van Wijngaarden's best-known contributions concerns the discovery of a slowly progressive autosomal dominant myopathy with joint contractures (Bethlem and van Wijngaarden 1976). In the nineties, this disease was shown to be genetically heterogeneous and to be a primary collagenopathy (Jöbsis et al. 1996). It now carries Bethlem's name.

The success of Bethlem and van Wijngaarden's outpatient clinic and the interest created by the reports in the literature on a great number of new neuromuscular diseases stimulated other Dutch neurologists to pay more attention to these diseases. Jaap Bethlem encouraged this development. Shortly before his 60th birthday he left the world of neurology and started another life.

THE EXPANSION

From approximately 1970 onwards, neurologists with a special interest in neuromuscular disorders made their appearance in staffs of neurology departments. In each neurological centre, the approach to neuromuscular diseases had some peculiar features depending on the physician who was primarily responsible. Hans J.G.H. Oosterhuis was predominantly interested in myasthenia gravis and made the department of neurology of Groningen University the national referral centre for myasthenia. Peter G. Barth of the Vrije Universiteit of Amsterdam owed his inclination to search for new x-linked diseases to a large pedigree with x-linked myotubular myopathy – the second in the Netherlands – which he had diagnosed early in his career, and subsequently discovered an x-linked cardioskeletal myopathy with abnormal mitochondria and neutropenia (Barth's disease) (Barth et al. 1981, 1999). He remained interested in childhood neuromuscular diseases. Ed M.G. Joosten and Anneke A. Gabreëls-Festen in Nijmegen, and Frans G.I. Jennekens in Utrecht took the lead in the investigation of diseases of peripheral nerves, and Herman F.M. Busch in Rotterdam concentrated on organelle diseases, together with the biochemist (Jasper) H.R. Scholte. Chris J. Höweler, also in Rotterdam, tackled a number of problems in myotonic dystrophy and continued his studies on this subject at the newly created university in Maastricht. Axel R. Wintzen in Leiden had a special interest in geriatric neuromuscular syndromes and J.M.B. Vianney de Jong in Amsterdam – the eldest son of Joop de Jong – continued and expanded the research initiated by Wim A. den Hartog Jager (1913-1993) on amyotrophic lateral sclerosis. The members of this generation remained in charge until approximately 1990. From then on, one by one, they were gradually succeeded by others.

Initially, most of these clinicians' experience with rare neuromuscular diseases was slight. Therefore, it was proposed to organise meetings for the exchange of information. From 1972 onwards, these meetings were, and still are, held twice a year. Soon they were also attended by clinicians and researchers from Belgian Universities and Jean-Jacq Martin of the Antwerp University became chairman of the Belgian-Dutch Neuromuscular Club, as it was then called, and remained so for many years. The Club became the vehicle for contact between clinicians and researchers and furthered collaboration and friendship.

The first official recognition for the work done in the field of neuromuscular diseases in the Netherlands came from University of Utrecht, which created a so-called 'special' professorate of neuromyology for Frans G.I. Jennekens in 1986. Amsterdam and Leiden followed with professorates for neuromuscular diseases.

THE INTERDISCIPLINARY GROUP FOR NEUROMUSCULAR DISEASES IN NIJMEGEN

For clinicians and scientists from other centres, the University of Nijmegen, located in the eastern part of the country, near the German border, was extraordinary, because it seemed to have more of everything: more outpatient facilities, more patients, more laboratories, more technicians and better instruments. The 'impossible' sometimes appeared easy in the department of neurology in Nijmegen. In 1970, at a congress for child neurology in Prague, the child neurologist Fons J.M. Gabreëls became fascinated by beautiful electronmicroscopic figures of storage material in peripheral nerve biopsies from children with Krabbe's disease and metachromatic leucodystrophy. Fons decided that he needed this new method in his own department. In the same year, he founded the Nijmegen Interdisciplinary Work Group for Neuromuscular Diseases and persuaded clinicians, neurophysiologists, biochemists, morphologists, cell biologists and geneticists to participate. From that date on, 'Nijmegen' diagnosed and advised more patients with neuromuscular diseases, and for many years produced more papers in better journals than any other centre in the Netherlands. Among the achievements of the Interdisciplinary Group are a long series of meticulous qualitative and quantitative studies of the light- and electronmicroscopy of nearly all the different forms of Charcot-Marie-Tooth and Dejerine-Sottas disease (see for example Gabreëls-Festen et al. 1999a,b; Gabreëls-Festen et al. 1993). Hereditary pressure neuropathy and cerebrotendinous xanthomatosis are key-topics of the group (Verrips et al. 2000a,b; Lenssen et al. 1998). Nijmegen is at present a referral centre for the western part of the European continent for mitochondrial disorders and has a special chair for these disorders.

NEUROMUSCULAR GENETICS: DUTCH INVOLVEMENT IN A MAJOR BREAKTHROUGH

Following the discovery of the gene for Duchenne muscular dystrophy in 1986, a kind of gold rush set in. At the end of the century, the gene locations of the major neuromuscular diseases were all known and many gene mutations had been identified. Gene mutations became the ultimate criteria for the diagnoses of hereditary diseases and allowed for improved genetic counselling. Geneticists from Leiden, Nijmegen and Amsterdam, closely collaborating with many neurologists, contributed significantly to gene discovery in at least nine neuromuscular diseases: Barth's disease (Bolhuis et al. 1991), Bethlem's disease (Jöbsis et al. 1996), Charcot-Marie-Tooth disease 1b (Kulkens et al. 1993), congenital spinal muscular atrophy (Van der Vleuten et al. 1998), hereditary pressure neuropathy (Mariman et al. 1994), Moebius syndrome (Kremer et al. 1996), myotonic dystrophy (Aslanidis et al. 1992), limb girdle dystrophy with cardiomyopathy (van der Kooi et al. 1997) and, above all, facioscapulohumeral muscular dystrophy (Wijmenga et al. 1991, Van Deutekom et al. 1993).

SOME OTHER ORIGINAL DUTCH CONTRIBUTIONS

What are the other main contributions by Dutch physicians to the research of neuromuscular diseases? The selection for this category would have been easier if the choice had been limited and if clinical or scientific discoveries had always been published in the *New England Journal of Medicine* or *Nature*. The present author takes full responsibility for the choice made here. My selection method was as follows: I carefully re-read the book *Neuromuscular Diseases* by de Visser et al. (1999), which contains descriptions of the main features of practically all neuromuscular diseases, and at each new entry I consulted my memory, trying to recall important Dutch developments and discoveries. Using PUBMED, I also examined the lists of publications by prominent Dutch authors. My criteria for selection were clinical research, novelty, potential impact, and publication before 2001. Finally, I decided that five other contributions should be mentioned.

Anticipation: in the first chapter of his doctorate thesis, Chris J. Höweler described how the Swiss ophthalmologist Fleisher (1874-1965) discovered 'anticipation' of clinical expression of myotonic dystrophy in subsequent generations of nine families. Fleisher's observations were published in 1918 and 1922 and initially confirmed by physicians but subsequently rejected by geneticists because they considered the findings to be due to bias and selection of families. Höweler decided to re-study the subject. After a painstaking investigation of 14 myotonic dystrophy families he convincingly showed anticipation to occur in 98 per cent of 61 index free parent-child pairs (Höweler 1986, Höweler et al. 1989). From that moment on, the phenomenon of anticipation became an undisputed fact. Anticipation in dominant transmission has since been demonstrated to be a characteristic feature in a series of diseases and has been shown to be related to an unstable gene mutation. Anticipation of a hereditary disease has considerable consequences for the genetic counselling of patients and carriers.

Chronic idiopathic axonal polyneuropathy: Within the category of difficult to diagnose neuropathies, there is a chronic axonal polyneuropathy of unknown origin

(CIAP or cryptogenic polyneuropathy) with onset in middle or old age. Until Nicolette C. Notermans started to study this condition, it had attracted only little attention. Though the incidence of CIAP is not known, it is likely to be among the most frequent disorders of the peripheral nervous system and affects males more often than females. She demonstrated that CIAP was more sensory than motor and that it had a slowly progressive course. Patients did not become severely disabled (Notermans et al. 1993, 1994). It was not a paraneoplastic syndrome, and it was not associated with any of the well-known monoclonal gammopathies (Notermans et al. 1996), nor was it simply caused by ischaemia (Teunissen et al. 2000). CIAP differed from hereditary motor and sensory neuropathy type 2 in having generally a later onset, more sensory symptoms and a more benign course (Teunissen et al. 1997). Patients with CIAP do not need to worry greatly and need no regular control laboratory investigations.

Critical illness polyneuropathy: a substantial number of patients in intensive care units are critically ill and suffer from multiple organ dysfunction. Most of them need artificial respiration and are treated during this period with neuromuscular blocking agents. Those who survive may be difficult to wean from the artificial respirator. They show evidence of a flaccid tetraparesis, areflexia and muscle atrophy. Sensory impairment is also present but is usually difficult to assess. The syndrome is due to an axonal polyneuropathy and a myopathy and recovers slowly in the months following the critically ill period. Dolf A.W. Op de Coul discovered this syndrome in the early eighties (Op de Coul et al. 1983), almost simultaneously with several other authors in other countries. His initial hypothesis that the syndrome might be due to pancuroniumbromide treatment was not confirmed. Shortly after his death, his collaborators provided evidence for a role of an immune mediated process (de Letter et al. 2000).

Intravenous infusions of immune globulins (IVIG) for inflammatory neuropathies: a 51-year-old man had acquired chronic inflammatory demyelinating polyneuropathy (CIDP) and became tetraplegic. He was treated with plasma exchange and could walk again within a matter of days. However, relapse followed. As retreatment with plasma exchange was not possible for various reasons, Herman F.M. Busch decided to treat him with infusions of fresh frozen plasma, and again the patient could walk within a few days. This effect was described in a letter (Maas et al. 1981) and a similar effect in a second patient was reported in a poster at a neuromuscular congress in Marseille in 1982 (Busch et al. 1982). The switch from plasma infusions to infusions of gammaglobulins was made by Marinus Vermeulen. In 1985, the favourable effect of plasma and gammaglobulin infusions on muscle weakness in CIDP was described in more detail (Vermeulen et al. 1985) and was subsequently confirmed by the same authors (van Doorn et al. 1990) and by others. Frans G.A. van der Meché et al. (1992) showed that intravenous immune globulin infusion in the Guillain-Barré syndrome was to be preferred to plasma exchange. IVIG is now the method of choice for treatment of acute and chronic inflammatory neuropathies.

Treating Pompe's disease: the special interest in Pompe's disease in Rotterdam dates from the doctorate thesis by M. Christa B. Loonen in 1979. The feasibility of enzyme therapy for Pompe's disease was investigated and led in 1989 to a positive conclusion (van der Ploeg et al. 1990). Recombinant human alpha glucosidase was then produced and shown to be effective in a mouse model of the disease (Bijvoet et al. 1999). In 2000, the first report was published about the improvement of skeletal and cardiac muscle function by enzyme therapy in children with Pompe's disease (van den Hout et al. 2000).

LIMITATIONS OF DUTCH RESEARCH AND CARE

A bibliometrical analysis of Dutch neuromuscular research in the years 1986 up to 1995 provides a few leads to limitations of Dutch neuromuscular research and care (Jennekens and Rutgers 1999). The Centre for Science and Technology Studies in Leiden had been asked to perform a literature search of publications on neuromuscular subjects by Dutch authors in international refereed journals. It appeared that Dutch authors had published at least 1036 articles, letters and reviews in the selected ten-year period. Overall, Dutch publications on neuromuscular disorders had been cited more often than articles from other countries worldwide in the same journals (ratio 1.32). Approximately 50 per cent of these publications were clinical, 19 per cent were experimental and the others were 'strategic'. Table II shows that the clinical studies addressed in particular features of diseases and diagnostic methods. The percentage of clinical publications that was dedicated to interventions seemed initially satisfactory. However, many of these publications appeared to be letters about previous Dutch trials or trials in other countries. Very few studies dealt with natural history and care.

Table II. Dutch publications on clinical research of neuromuscular diseases, 1986-1995. Percentages in 7 sub-fields.

Cause of diseases	Mechanisms underlying diseases	Features of diseases	Diagnostic methods	Natural history	Studies about intervention	Care
4%	12%	46%	20%	2%	18%	1%

In the period investigated, Dutch neuromuscular clinicians were certainly not on the forefront in knowledge and experience of intervention studies. This is probably in part due to the limited number of patients suffering from any one neuromuscular disease. Since 1995, the problem has to some degree been remedied by close collaboration of different centres and by support of clinical epidemiologists in methodological problems, but it remains difficult to perform intervention studies on diseases such as Duchenne muscular dystrophy within the confines of a small country (see section on recent developments). The low percentage of studies on natural history may reflect the difficulty of such investigations in slowly progressive diseases. Care research had been performed in amyotrophic lateral sclerosis (Mathus-Vliegen et al. 1994), but otherwise not much work had been done in this field. Two developments announce a new period in this respect: improved funding of care research and specialisation of nurses in specific neuromuscular diseases.

Neuromuscular organisations

THE DUTCH SOCIETY FOR MUSCLE DISEASES (VERENIGING SPIERZIEKTEN NEDERLAND)

Fried Huisinga-Nijsen in Leeuwarden, mother of a boy with Duchenne muscular dystrophy, and Ysbrand S. Poortman in Baarn, father of a girl with autosomal recessive hereditary spinal muscular atrophy, took the initiative to found the 'Parent Committee for Children with Muscular Dystrophy' in 1966. Ysbrand Poortman became the director of this organisation, which subsequently became denoted by its present name (Fig. 4). It is now the umbrella organisation for all groups of patients with muscle diseases, including patients with postpolio syndrome and amyotrophic lateral sclerosis. The VSN has gradually become quite influential, not only in the organisation of mutual support of patients but also in medical matters. The following are just a few examples. The VSN felt that respiratory support – at home or in another adequate environment – should be available for neuromuscular patients who wished to be so treated and strived to realise this option from 1969. In the course of the eighties, it succeeded. Chronic respiratory support is now available without financial restriction for everyone who needs it. The VSN organised a network of rehabilitation centres with special interest in neuromuscular diseases. It stimulated timely surgical correction of scoliosis in children with neuromuscular diseases. The VSN assisted and stimulated Dutch neurologists involved in care and research of neuromuscular diseases in improving their cooperation and it did its utmost to help maintain outpatient clinic facilities for neuromuscular patients throughout the country in all large medical centres.

Figure 4. Ysbrand S. Poortman, one of the founders of the Dutch Society for Muscle Diseases (Vereniging Spierziekten Nederland) and its first director. He was essential in the founding of the European Neuromuscular Centre and of the European and World Associations for Muscle Diseases (EAMDA and WAMDA).

FUNDING OF DUTCH NEUROMUSCULAR RESEARCH: THE PRINSES BEATRIX FONDS

There is no denying that neuromuscular research is predominantly paid for by the government, either directly or via a state-financed organisation ('Dutch Scientific Research') but that is not all. Young scientists, engaged in preparing and writing their doctorate thesis (comparable to but not the same as a Ph.D.) are often subsidised by the Prinses Beatrix Fonds, which has played a key role in Dutch neuromuscular research since approximately 1970.

The Prinses Beatrix Fonds was initially founded to help victims of poliomyelitis. When vaccination programmes became effective and poliomyelitis rare, Jaap Bethlem convinced the Prinses Beatrix Fonds that it would find another interesting and important task in stimulating research of neuromuscular diseases and some idiopathic and metabolic brain diseases. Visitors from other countries will therefore not see any placards here inviting them to donate to muscular dystrophy or motor neuron disease organisations, though they could be approached by volunteers asking for a donation to the Prinses Beatrix Fonds. The Prinses Beatrix Fonds is essential for the Dutch neuromuscular community. It finances both the VSN and Dutch neuromuscular research for a considerable part.

FOUNDATION FOR NEUROMUSCULAR RESEARCH AND THE RESEARCH SUPPORT GROUP

In approximately 1985, clinicians, scientists and representatives of the VSN took the initiative for the foundation of a formal organisation to stimulate neuromuscular research and to spread knowledge about the neuromuscular diseases. This 'Foundation for Neuromuscular Research' organises postgraduate courses, publishes a bulletin twice a year and has an executive secretariat that is known as the Research Support Group (Interuniversitair Steunpunt Neuromusculair Onderzoek = ISNO). The Foundation has asked the Netherlands Society of Neurology and the Order of Medical Specialists to create the opportunity for neurologists to obtain a certificate in neuromuscular diseases. This implies that candidates are offered the opportunity to train in neuromuscular diseases for an additional twelve-month period in one of the Dutch neuromuscular university centres. The request was granted in 2000. ISNO organises meetings to draw up diagnostic criteria and guidelines for diagnosis and treatment of neuromuscular diseases and it organises congresses.

RECENT DEVELOPMENT IN RESEARCH

The Netherlands is a reasonably well organised small country of 36.000 km^2 and has a population density of approximately 450 inhabitants per km^2. These characteristics favour nationwide investigations. Though single university projects are manifold, the present generation of clinicians and researchers tends to participate in multicentre projects (Table III).

Nationwide investigations have revealed how rare some of the neuromuscular diseases are. By 1995, there were 139 symptomatic facioscapulohumeral muscular dystrophy kindreds in the Netherlands, 36 of which were sporadic cases. There were 105 limb girdle muscular dystrophy (LGMD) patients ($8.1/10^6$) and at least 76 ($4.9/10^6$) patients with inclusion body myositis (IBM). Data about the incidence and prevalence of other diseases are to be expected in the near future from a nationwide registration system initiated by Baziel G.M. van Engelen. The most widely known intervention studies from the period before 1995 are probably the trials on the effect of immune globulins in the Guillain-Barré syndrome (see section on Original Dutch

Table III. Examples of multi-centre investigations since 1995.

Universities	Senior responsible authors	Subject	Main references
Amsterdam	De Visser M.	LMGD. Prevalence, types	Van der Kooi A.J.
Amsterdam and Utrecht	De Visser M., Hoogendijk J.	Myositis, Types, intervention	Van der Meulen M.F.
Groningen	Fock J., vd Hoeven J.	Duchenne. Intervention	
Leiden	Wintzen A.	IBM. Prevalence, intervention	Badrising U.A.
Leiden	Verschuuren J.	LEMS. Prevalence, intervention	
Nijmegen	Van Engelen B	NMD. Registration, country wide	
Nijmegen and Leiden	Padberg G.	FSHD. Prevalence, intervention	Padberg G.W
Rotterdam	Van der Meché F.	Guillain-Barre. Interventions	Dutch Guillain Barré Study Group
Rotterdam	Van der Ploeg A.	Pompe. Intervention	Van den Hout H.
Utrecht	Notermans N., Wokke J.	MGUS neuropathy. Intervention	Notermans N.C.
Utrecht	Van den Berg L., Wokke J.	ALS. Interventions	
Utrecht and Amsterdam	Wokke J., de Visser M.	PSMA. Prevalence, natural history	
Utrecht	Van den Berg L., Wokke J.	MMN. Intervention	Van den Berg L.H.; Van den Berg-Vos R.M.

Abbreviations: ALS=amyotrophic lateral sclerosis; FSHD=facioscapulohumeral muscular dystrophy; IBM= inclusion body myositis; LEMS= Lambert-Eaton myasthenic syndrome; LMGD= limb girdle muscular dystrophy; MGUS =monoclonal gammopathy of unknown significance; MMN=multifocal motor neuropathy; NMD= neuromuscular diseases; PSMA=progressive spinal muscular atrophy

Contributions) and on acetylcysteine in ALS (Louwerse et al. 1995). Since the completion of these trials, many other intervention studies have been initiated. All of them are based on multicentre cooperation.

Summary

Once Bethlem and van Wijngaarden had started their outpatient clinic for myopathies in the early 1960s in Amsterdam, the interest for neuromuscular diseases spread among neurologists in the country. Clinical research was initially directed at the development of diagnostic methods and the discovery of new neuromuscular diseases. DNA technology provided a golden standard for the diagnosis of neuromuscular diseases. Prevention of hereditary neuromuscular diseases improved by genetic counselling. Gradually, clinical research moved from diagnosis-related topics to epidemiological aspects and treatment strategies. In the course of the last decade, the number of intervention studies has increased steadily. Projects with a nationwide scope have become quite common. The well-being of patients with chronic neuromuscular diseases has become an important issue and has led to the introduction of symptomatic therapies and to care-research. Despite the often impressive progress made in several fields, causal therapies are still not available for most hereditary diseases and some acquired disorders.

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Neuropsychology

15

The Early History

J.A.M. Frederiks

What is neuropsychology? Neither a precise and exact nor a generally accepted definition is to be found in the pertinent literature. In the editorial of number one, volume 1, of the new journal *Neuropsychologia* (1963), the following definition was given: "Under the term 'neuropsychology', we have in mind a particular area of neurology of common interest to neurologists, psychiatrists, psychologists and neurophysiologists."

In fact, neuropsychology studies clinical phenomena that arise from disorders of the central nervous system, in so far as these affect the sphere of consciousness and behaviour. Accordingly, neuropsychology does not lie within the confines of neurology and psychiatry, but in between neurology and psychology, or, more correctly, between the domain of the neurosciences and that of the behavioural sciences. In short, neuropsychology is the study of normal and pathological relationships between the brain and behaviour (Frederiks 1985). It includes topics such as aphasia, apraxia, agnosia, amnesia, hallucination, reading and writing disorders, learning disabilities, disorders of the body schema, disorders of consciousness and attention, and disorders of higher nervous activity in old age.

Initially, until about 1950, neuropsychological topics were studied mainly by a few talented clinical neurologists, including Broca, Wernicke, Meynert, Kleist, Goldstein and Head; thus, neuropsychology was born and had its cradle in the neurological clinic (Hécaen 1980). World Wars I and II, in particular, supplied a vast amount of material for research, and psychologists studied groups of these war casualties with brain lesions with the aid of numerous psychological tests. This had the extra advantage of excluding diseased or aged patients from the study, but including a more homogenous category of young healthy males in whom localised brain injury had been inflicted by bullets, shrapnell or stabs. Within that context, reference should be made to Goldstein, Zangwill, Teuber, Milner, Hécaen, and Luria.

In a foreword to Henri Hécaen's *Human Neuropsychology* (1978), Geschwind pointedly summarised the early history of neuropsychology:

> Before World War I this field occupied a central position in neurology, and nearly all the great figures who created the discipline made contributions to the understanding of the more advanced functions of the human brain. After the Great War, however, there was a sharp decline in interest, and only a corporal's guard of isolated and courageous scholars maintained the fragile thread of the great tradition. At the end of World War II only a handful of investigators were devoting themselves to this area. Henri Hécaen was one of the new pioneers who revived the field.

The present chapter surveys the origins and development of neuropsychology in the Netherlands up to the 1970s. In view of the framework of this book, most attention will be paid to the contributions by neurologists. Since the mid-1970s neuropsychology has become mainly the remit of psychologists specialised in that field and accordingly denoted as neuropsychologists.

In considering this history, one is struck by its parallels with the historical developments in neuropsychology abroad. Both in the Netherlands and in foreign countries, virtually all early contributions to neuropsychology stemmed from neurologists. The development of an interdisciplinary neuropsychology, essentially participated in by psychologists, is of a relatively recent date (Hécaen 1980, Hagner 1996). At present, it is self-evident to everyone that neuropsychology is practised by neurologists, neuropsychologists, neurophysiologists, neurolinguists, perception and behaviour scientists, often in close collaboration.

Compared to other European countries and the United States, the situation in the Netherlands differed, however, in some respects. In some other countries the interest in neuropsychological topics exceeded ours, their neuropsychological publications outnumbering ours. In addition, the Dutch did not harvest such extensive experience with patients with brain injuries from World War I (in which we stayed neutral bystanders) and World War II.

The term 'neuropsychology' came into current use in the early 1960s, especially through the work of one of its founding fathers, the French neurologist Henri Hécaen (1912-1983), who named his Paris laboratory 'Groupe de Neuropsychologie et de Neurolinguistique', and who, with others, founded the 'International Neuropsychological Symposium' (Boller 1999).

Four different authors should be given credit for the initial use of the term 'neuropsychology': Sir William Osler (1849-1919) in 1913, Kurt Goldstein (1878-1965) in 1934, Karl Lashley (1890-1958) in 1936, and Donald Hebb (1904-1985) in 1949. The discussion on this topic seems to be decided in favour of Osler (Bruce 1985; Benton 1988; Finger 1994). In the present author's opinion there are good reasons to single out Goldstein; the choice depends on the emphasis and context by which the word was used by the different authors. Initially, the term 'disorders of higher nervous activity' was also in use. This term disappeared without further comment: until that time nobody had defined the interpretation of 'disorders of highest activity'!

The foundation of two new journals, *Neuropsychologia. An International Journal* (Oxford) in 1963 (by Henri Hécaen et al.) and of *Cortex. A Journal Devoted to the Study of the Nervous System and Behavior* (Milan) in 1964 (by Ennio de Renzi and others), clearly marked the start of international cooperation during these years.

Early contributions by psychologists, to what would later be called neuropsychology, originated mainly from experimental psychologists. In the Netherlands, the first psychologist to be mentioned in this respect is Gerard Heymans (1857-1930), professor of psychology and philosophy at the University of Groningen from 1890-1927. This 'founder of psychology in the Netherlands' (Van Strien 1993) established, in imitation of the physiologist Wilhelm Wundt (1832-1920) in Leipzig, his nationally well-known Psychological Laboratory in 1892. This 'laboratory for the soul' (Draaisma 1992) marked the beginning of experimental psychology in the Netherlands.

In an oration entitled 'The coming century of psychology' (Groningen, 1909), Heymans sketched the nineteenth century as the century of the natural sciences, and the 'coming' (twentieth) century as the century of psychology. It is remarkable that, a further 100 years later – in 2000 – the just started 21st century was named the 'century of cognitive neuroscience' by Peter Hagoort, in an oration on the occasion of his inauguration as professor of Neuropsychology in Nijmegen (Hagoort 2000). Things have changed rather quickly indeed! And in fact, in the late 1950s, early 1960s one occasionally heard the term 'cognitive revolution' (Halligan and Marshall 1997).

Other precursors of Dutch neuropsychology were the physiologist F.C. Donders (1818-1889), the psychologists G. Révèsz (1878-1955) and Abraham Grünbaum (1885-1932), the physician, physiologist and psychologist F.J.J. Buytendijk (1887-1974), and the physiologist G. van Rijnberk (1875-1953).

'Clinical psychology' may be regarded as another early historical step towards (clinical) neuropsychology. The development of this sector of psychology was gradual and took place in the 1940s and 1950s (van Strien 1993). Workers in the field of psychiatry strove for collaboration with psychologists. Initiator was Prof. Prick in Nijmegen, soon followed by Prof. Rümke in Utrecht, Prof. L. Bouman (Vrije Universiteit Amsterdam, later Utrecht) and Prof. Grewel (University of Amsterdam) (Prick 1947; Van Strien 1993).

In the 1950s and 1960s, the practice of neuropsychology by a small number of psychologists gradually came into being. Psychologists were no longer content with the attainments of introspection and behaviourism and turned to the neurosciences, and the natural scientific-basis of cognitive functions. An abundance of neuropsychological activities by psychologists gradually arose in the 1970s (e.g., D.J. Bakker, A. Bouma, B.G. Deelman, H.R. van Dongen, A.H. van Zomeren, H. van der Vlugt).

The relatively late Dutch emergence of neuropsychology by psychologists is reflected by the publication, in the 1970s, of books on the history of Dutch psychology without treating the subject of neuropsychology; the word neuropsychology was not even mentioned (Verbeek 1977; Eisenga 1978). Even a recent book on the history of Dutch psychology ignores the field of neuropsychology completely (Van Strien 1993). The quickening of activities of psychologists in this field is of a relatively recent date.

There is another way to demonstrate this transition. In 1964, the Dutch journal of psychology (*Nederlands Tijdschrift voor Psychologie*) published a thematic issue on neuropsychology. The authors were almost exclusively neurologists. Twelve years later, in 1976, the same journal published another thematic issue on neuropsychology, but now exclusively written by psychologists.

Publications

The early contributions to neuropsychology by Dutch neurologists were quite different from those by psychologists. Their writing on topics such as aphasia, apraxia, agnosia, dyslexia, agraphia and cerebral localisation was inspired by their experience with neurological patients. In their days, examining patients with disorders of higher nervous activity was part of a thorough clinical examination of patients with diseases of the central nervous system.

The publications by Dutch neurologists on neuropsychological topics reflect much of the development of their contribution to neuropsychology in the Netherlands. Table I gives a list of theses up to 1970. The very few early theses by Dutch neurologists on neuropsychological topics differ quite a bit from actual theses. The thesis of Van Rhijn on aphasia (Leiden, 1968), for example, contains only a brief description of three case histories, but rather extensive discursive considerations without engagement. Of course, the quality of theses evolved later with the growing knowledge of that time. And of course, during the first 70 years of the 20th century many papers on neuropsychological themes were published in Dutch and foreign journals. Of the Dutch journals we mention the Dutch medical weekly (*Nederlands Tijdschrift voor Geneeskunde*) and the Dutch journal of Psychiatry and Neurology (see also chapter 6).

In the first half of the twentieth century (up to 1960), one frequently notes papers by the following authors (in alphabetical order, but as a matter of course, without being complete): A. Biemond (visual agnosia, see also chapter 17), L. Bouman (aphasia, apraxia), J.G. Dusser de Barenne (cerebral localisation, see also chapter 20), A. Gans (apraxia, aphasia, astereognosia), F. Grewel (aphasia, neurolinguistics, acalculia, see also chapter 21), K. Heilbronner (aphasia, apraxia, asymbolia, agraphia, stammer), L. van der Horst (constructional apraxia), G. Jelgersma (aphasia, apraxia, see also chapter 22), D. Moffie (aphasia, parietal lobe pathology), J.J.G. Prick (aphasia), V.W.D. Schenk (dyslexia and dysgraphia in children, aphasia, neurolinguistics), H.W. Stenvers (aphasia, alexia, agraphia, see also chapter 26), C.T. van Valkenburg (cerebral localisation, aphasia, apraxia, central sensory representation, body image, see also chapter 27), C. Winkler (cerebral localisation, aphasia, see also chapter 30), and W. van Woerkom (aphasia).

Up to the 1970s a few books on neuropsychological topics were published. The neurologist A. Verjaal wrote *Agnosia Aphasia Apraxia* (1950), a small introductory guide to neuropsychological examination. During the 1970s a small introductory book on neuropsychology, written by the neurologist A. Welman, was popular in the Netherlands: *Hoofdstukken uit de klinische neuropsychologie. Afasie, apraxie, agnosie* ['Chapters from clinical neuropsychology. Aphasia, apraxia, agnosia'] (first edition 1974, second edition 1979).

The multi-volume *Handbook of Clinical Neurology* (editors: P.J. Vinken & G.W. Bruyn; Elsevier, Amsterdam) includes four volumes implicitly or explicitly dealing with neuropsychological topics (editor: J.A.M. Frederiks) : Disorders of Higher Nervous Activity (volume 3, 1969), Disorders of Speech, Perception, and Symbolic Behaviour (volume 4, 1969), Clinical Neuropsychology (volume 45/1, 1985), and Neurobehavioural Disorders (volume 46/2)

Table I. Theses by Dutch physicians/neurologists on neuropsychological subjects up to 1970 (in chronological order).

A. van Rhijn: Aphasie (promotor: prof. Dr J.A. Bogaard) Leiden, 1868.
[thesis on aphasia]

Aletta Jacobs (physician): Over lokalisatie van physiologische en pathologische verschijnselen in de groote hersenen (promotor: Prof. H. Kooyker), 1879.
[thesis on cerebral localisation]

J.K.A. Wertheim Salomonson: Stereognosis (promotor: ?) Leiden, 1888.
[thesis on astereognosia]

M.A. van Melle (physician and philosopher): Over aphasie (promotor: Prof. Dr C. Winkler) Amsterdam, 1900.
[thesis on aphasia]

D.M. van Londen: Onderzoek naar den duur der eenvoudige psychische processen v.n. bij de psychosen (promotor: Prof. Dr C. Winkler) Amsterdam, 1905.
[thesis on duration of elementary psychical processes]

A. Gans: Over tastblindheid en over de stoornissen van de ruimtelijke waarnemingen der sensibiliteit (promotor: Prof. Dr C. Winkler) Amsterdam, 1915.
[thesis on astereognosia]

M. van der Reis: De omvang van het bewustzijn bij gezonden en geesteszieken (promotor: prof. Dr E.D. Wiersma) Groningen, 1924.
[thesis on consciousness in health and disease]

H.G. van der Waals: Optische schijnbewegingen (promotor: Prof. Dr K.H. Bouman) Amsterdam, 1927.
[thesis on optic illusionary movements]

W.J. Smit: Phantoombelevingen (promotor: Prof. Dr L. Bouman) Utrecht, 1933.
[thesis on phantom limb]

A. Verjaal: Amnesie na trauma capitis. Een klinisch-psychologische bijdrage tot de kennis der omschreven geheugenstoornissen (promotor: Prof. Dr H.C. Rümke) Utrecht, 1938.
[thesis on posttraumatic amnesia]

R. Vedder: Over het copieeren van eenvoudige geometrische figuren door oligophrenen en jonge kinderen (promotor: Prof. Dr H.C. Rümke) Utrecht, 1939.
[thesis on constructional apraxia]

W. Noordenbos (neurosurgeon): Pain (promotor: Prof. Dr A. Biemond) Amsterdam, 1959.
[thesis on pain]

A.J. Welman: Psychodiagnostisch onderzoek bij patiënten met een hersengezwel (promotor: Prof. Dr E.A.D.E. Carp) Leiden, 1961.
[thesis on psychodiagnostic examination of patients with brain tumour]

J.A.M. Frederiks: Het lichaamsschema. Een klinisch-theortische studie (promotor: Prof. Dr A. Biemond). Amsterdam, 1961.
[thesis on the body scheme and its disorders]

H.J.A. Verhagen: Dyslexie en dyscalculie (promotor: Prof. Dr W.G. Sillevis Smitt) Utrecht, 1968.
[thesis on dyslexia and dyscalculia]

Organisation

In the Netherlands, the interdisciplinary character of neuropsychology came of age at the time when, at a clinical level, neurologists and other neuroscientists developed an intense cooperation with psychologists. As in other countries, this occurred at first timidly in the 1960s, but at a higher and intense level and at a rapid pace in the 1970s. At present, neuropsychology is an established discipline, practised chiefly by trained (neuro)psychologists.

Dutch neuropsychology has been organised in different ways. Local and international activities can be summarised as follows.

In 1955, the neurologist F. Grewel was the local organiser of the 5th Meeting of the International Neuropsychological Symposium in Amsterdam.

In November 1963, F. Grewel and A.J. Welman founded an interdisciplinary 'Study and Work-group for Neuropsychology'. Membership was open to neurologists, psychologists, psychiatrists and speech therapists. From an international point of view, the Netherlands was certainly not late with this establishment.

In October 1968, this work-group was converted into a definite interdisciplinary 'Netherlands Society of Neuropsychology'. Its board consisted of J.A.M. Frederiks (chairman), A.J. Welman (secretary), and the psychologist B.G. Deelman (treasurer). This society grew steadily into a large interdisciplinary association (Eling 1996, 1997) with 825 members at present (2001;information of the secretary of the society). Foreign contacts were maintained for example via visits to the 'International Neuropsychological Symposium' and to the 'International Neuropsychological Society' founded in 1965 (Rourke and Murji 2000). During the first years of its existence, Eberhard Bay from Düsseldorf and Henri Hécaen from Paris were stimulating visiting speakers.

It was felt that there was a need to improve and enlarge the basis of scientific training, and so a special section of neuropsychology was founded as part ('section') of the Netherlands Society of Psychiatry and Neurology, a section that would facilitate the inclusion of neuropsychological information in the training and practice of neurologists and psychiatrists. The section was founded on May 29, 1969. The first board consisted of J.A.M. Frederiks (chairman), A.J. Welman (secretary), and F. van Harskamp (member). The section maintained, by its very nature, close contacts with the Netherlands Society of Neuropsychology.

Behavioural neurology

After 1970, neuropsychology gradually became mainly a topic for (neuro-)psychologists, although its interdisciplinary pillars have never been lost. With their validated and standardised tests neuropsychologists offered a substantial contribution to clinical problems. In the same period, a new, 'robust, powerful' sub-speciality of neurology gradually emerged: behavioural neurology (Benson 1993, 1996). The need for this speciality became evident in the mid-1970s, after the practice of psychiatry and neurology became separated. "Whether an independent position can be retained for neuropsychiatry is open to question"; the position of behavioural neurology is stronger (Benson 1996).

Taken together, it looks as if, in the short term, neuropsychology will remain the domain of (neuro-)psychologists and behavioural neurology that of neurologists (Benson 1996).

Concluding remarks

The contemporary period again shows an intense interdisciplinary collaboration with neurologists and other neuroscientists. The advanced techniques of imaging such as CT, MRI, fMRI, PET, and rCBF are central to this concerted action (Hagoort 2000).

It is perhaps under these circumstances that the words of D.O. Hebb (1983) promise to be a new reality: ."‥ the neuropsychologist of the future must be psychologist as much as neurologist." In other words, an intense collaboration of the two disciplines will become more necessary than ever. And, if the science of neural networking, information theory, and 'cognitive electronics' pursues its present path, one can imagine that by the 21st century, both psychiatry and neuropsychology will have been re- absorbed by neurology.

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C.U. Ariëns Kappers *1877-1946* 16

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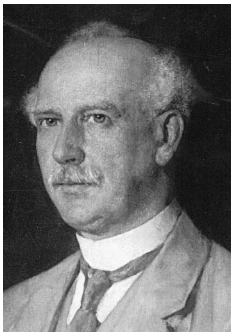

Figure 1.
C.U. Ariëns Kappers.

The figure of C.U. Ariëns Kappers, towering above the fairly flat landscape of today's Dutch neurosciences, constitutes an appetite-whetting challenge for any biographer who is not content with purely sketching descriptive outlines of the life and work of the subject. The scope and depth of the biographer's tale depend on his estimation of the readers' expectations as much as on how much energy the biographer is willing to expend on probing the interior of the person behind the exterior, and on gathering records and data, in order to present a reasonably integrated and harmonious portrait.

No sinecure indeed, particularly in the present case. On closer look, 'C.U.' (as we will denote him) appears to have been a complicated person, like C.T. van Valkenburg. Therefore, we might best aid the reader (and ourselves) by sketching the explicit contours of his life and work in some detail first, and then attempt to add to such a skeleton the implicit (though largely inferred) sinews, arteries and muscles of the living person. A full and definite biography, requiring years of interviews and archival-bibliographic research, remains to be written. It may well correct the historian's scientific reconstruction, not so much the dry record of what has been said and done, but rather what has not. Most of the pages below are based on printed sources, among them the autobiography, condensed by Van Kolfschooten (2001).

C.U. was born in the city of Groningen on August 9, 1877, into a family in which academic education, and the penury that usually went hand-in-hand with it, was the rule rather than the exception. He was the second of three sons. His paternal great-grandfather (surname Kappers, first names Johannes Arjen) was a village physician in the province of Groningen, subsequently combining the function of general physician with that of burgomaster. He had one son (C.U.'s grandfather) who, after his academic study in Groningen, ran a chemist there. One of his sons (C.U.'s father) studied physics and mathematics and successfully defended first a doctor's thesis on oxidation and subsequently a second one in pharmaceutics. He obtained a position as a teacher in chemistry and botany at the Higher Burgher School (HBS) and one of regional school inspector, first in the town of Sappemeer, later in the town of Meppel, and ultimately in Leeuwarden, the capital of the province of Friesland, where he was appointed as director of the HBS. His career at the university and his professional career show a man of drive and ambition.

The name 'Ariëns' probably stems from his great-grandfather: the grandfather, being 'Arjen's son', presumably used the customary abbreviation 'Arjens' and the father may have changed 'Arjens' to 'Ariëns', using the original first name as an additional surname.

After the family's move to Leeuwarden, C.U.'s performance at school proved to be insufficient for him to be admitted to the first form of the HBS there, so he had to repeat the final two years of the elementary school. The first three years at the HBS, too, taxed his capacities, especially the subject of mathematics. However, as is often seen in male pubescence, a sudden mushrooming of mental and cognitive faculties occurred, and he passed the final two years of HBS with flying colours, particularly in the subject of mathematics, obtaining his diploma in 1895. His ambitious father incited him to spend an additional year at the Gymnasium to acquire knowledge of Latin and Greek, because a Gymnasiumdiploma was requisite for enrolling at university and entering university exams. (The Limburg Act allowing HBS pupils to apply for university admittance was not passed in parliament until 1917, some twenty years later). Having obeyed paternal wishes, C.U. enrolled in the Medical Faculty of Amsterdam in October 1896. This university was probably chosen because C.U.'s elder brother, who had studied commerce in Duisburg (Germany), worked and lived in Amsterdam.

After the candidate exam in the fourth year of the curriculum, C.U. spent the afternoons in the laboratory of the histologist Prof. J. van Rees, because he wanted to become technically skilled in making microscopical preparations, especially the Ehrlich, Golgi, and Weigert stain techniques. In those years, the soaring flight of neuroanatomy and the new neuron-theory cannot have left the young student unmoved. C.U. went to Prof. C. Winkler asking him to pass judgement on his efforts and to coach him. Winkler alerted him to a student contest, offered by the University of Utrecht, which involved writing an essay on the development of nerve-sheaths, and the winner of which was to be awarded with a gold medal. Winkler offered him the use of his laboratory in the Binnengasthuis. C.U. won the gold medal, passed his B.M. ('doctoral' or 'masters' exam) soon after, and applied to the Committee of the famous Zoological Station at Napoli to work there during the winter months. He took lessons in Italian and volunteered to work on the information desk at the International Congress of Criminal Anthropology (Amsterdam, September 1901), where C. Lombroso, E. Ferri, Sc. Sighele, G. Sergi and C. Parnisetti were the leading speakers. He thus established the appropriate connections, which produced invitations from these gentlemen to come and visit them should he come to Italy.

Thanks to a government grant, C.U. indeed left for Italy in October 1901 (having passed his 'semi-arts' exam) and was the guest of Lombroso in Torino, of Parnisetti in Alessandria, and occupant of the Dutch desk in Napoli. There, he regularly met the leading Hungarian neurohistologist Stefan Apàthy and the Estonian-born neurophysiologist Jakob, Count von Uexküll, colloquially known as 'the nerve-shaker', recipient of the *honoris causa* doctorate of the University of Utrecht.

Clearly, the sparkle conveyed by his father had kindled the *feu sacré*. The gifted young man deployed a mass of energy: he passed the physician's licence exam on October 30, 1903, obtained a position as an assistant to Prof. J. Rotgans (pathological anatomy) in the Binnengasthuis, continued Teleosts' and Selachii's histological work on the motor nuclei of the brainstem for his MD thesis (promotor: Prof. J. van Rees), and applied again (successfully) to work in the Zoological Station in Napoli immediately after he had obtained the MD degree (*cum laude* [with honours] on November 11, 1904). He worked in Napoli from November 1904 to May 1905. On his way to Napoli he stopped over in Frankfurt to visit Ludwig Edinger, the founder of comparative neuroanatomy, at the Senckenbergisches Institut and presented him with an English translation (already!) of his thesis and a report of his work at the Napels Station. Clearly, his inclination towards comparative neuroanatomy directed his energies and he had already made the decision not to become the physician for which the university had trained him, nor to specialise as a clinical neurologist caring for the ill.

His efforts soon made his star ascend. C.U. was appointed 'privaat-docent' (i.e. associate professor) in Histology in Amsterdam, August 1905. His lectures attracted more students than those read by his promotor and supervisor, the ordinarius Van Rees, as a result of which tensions arose. The situation (classic in university circles between the receding old and the advancing young) was solved smoothly by the arrival of Edinger's offer to C.U., to become assistant at the Senckenbergisches Institut. Following consultation with Winkler and Van Rees (the latter being undoubtedly relieved to see the young rival go), C.U. left for Frankfurt in August 1906 and soon became a departmental manager there. Prof. J.B. Johnston, anatomist in Virginia and author of *The nervous system of vertebrates*, translated C.U.'s thesis, which was published in the *J. Comp. Neurol.* in 1906, in the fifteenth year of the journal's existence.

During the two years with Edinger, C.U. worked undisturbed and could assimilate the pertinent neuroanatomic literature which revealed a field in rapid evolution. Here, the thoughts he had vaguely formulated and started to direct with his doctoral thesis, were fertilised by Cajal's observations (of which he may have been aware) that the outgrowth of dendrites proceeds in the direction of arriving (afferent) stimuli, and matured by his work in Edinger's laboratory. A grand, central idea struck him suddenly in a synthesis of apparently heterogeneous and incoherent data: the concept of neurobiotaxis. This idea lifted well-known neuroanatomical findings to the higher level of neuromorphology, as Bolk so aptly put it in a speech ten years later. C.U. published the idea in the *Neurologisches Centralblatt* and read the first paper on it in the same year at the first International Congress of Psychiatry and Neurology in Amsterdam, September 1907. The concept, to which we will recur below, made his name.

The neurobiotaxis-concept overshadows his later work, such as his studies on the problem of mechanical versus functional causation of the phylogenetic increase of cortical convolutions. C.U. perceptively pointed out that the folding of grey matter not only increases at the brain's exterior surface but also in its interior (olivary nucleus, dentate nucleus, geniculate body, optic tectum, reptilian lamellar nucleus). Even his then authoritative three-volume text on the comparative neuroanatomy of vertebrates, translated into various modern languages (nowadays replaced by Nieuwenhuys' *nec plus ultra* text), only confirmed C.U.'s international repute, but did not transcend, like the neurobiotaxis-theory, from the neuroanatomical to the neuromorphological level of sophistication, i.e., from the descriptive to the interpretative. C.U. was to reap a richer harvest still.

In 1908, in concert with Winkler, the inveterate bachelor and workaholic Bolk, arguably the greatest Dutch (neuro-) anatomist ever, inquired by letter of Edinger whether C.U. was a suitable candidate to head the new Central Institute for Brain Research in Amsterdam. In the Supervising Committee of the Royal Academy of Sciences, Bolk, Winkler, Van der Waals (of the intra-atomic forces) and Von Wijhe agreed and it thus came to pass that C.U. was appointed Director at the festive opening of the Central Brain Institute, Amsterdam, on Tuesday June 9, 1909. C.T. van Valkenburg and Ernst de Vries were appointed deputy-director and assistant, respectively. Famous Waldeyer (of the neuron-theory), Winkler and C.U. read the official addresses (see *Algemeen Handelsblad* 1909, June 8, 82, page 1).

During the next decade or so he steadily enlarged the Institute's collection of vertebrate cerebra, and published well over 30 papers, the majority of them on neurobiotaxis, some of them on the brain of lower vertebrates, a few in books by others, as well as obituaries and eulogies on Victor Horsley, Ludwig Edinger, Arthur van Gehuchten and Cornelis Winkler. Remarkably, his early bibliography also includes two papers listing all medical journals held by Dutch libraries, testifying to the depth and scope of the meticulous documentation that underlies C.U.'s *magnum opus*.

The first edition of that study appeared in 1920. It was made in collaboration with Aemilius Bernard Droogleever Fortuyn (born 1888), a young colleague who succeeded Ernst de Vries in the Brain Institute from 1911 to 1913, became senior lecturer in Histology in Leiden, went to the Peking Union Medical College in 1923, and left with his wife, a biologist, for the USA in 1941. As sole author, C.U. elaborated the text into a two-volume book, in German in 1920/1921. A three-volume edition appeared in English in 1936 (reprinted in 1960 and 1967 posthumously) thanks to the nine years of translation and updating work carried out by Elisabeth Crosby in particular and also Carl Huber, which reflects the spell of charm C.U. had cast upon them. A French translation by E.H. Strasburger rolled off the printing presses in 1947 (again posthumously). All this established C.U.'s international authority on comparative neuroanatomy for three quarters of a century.

C.U. was awarded the Tilanus-medal by the 'Genootschap voor Natuur-, Genees-, en Heelkunde' [Association for natural and medical science and surgery] in 1915, and became member of the Dutch Royal Academy of Sciences in 1920. He went on an extensive trip to China to give a course of lectures in anatomy at the American sponsored Peking Union Medical College (1923-1924), returning via Manchuria, Korea, Japan and the USA, collecting the brain of a whale and brains of Japanese for the Amsterdam Institute. In the USA, he contacted well-known neuroanatomist C. L. Herrick (1858-1904; of the eponymous Herrick's cells and Herrick's commissure) who, together with his younger brother, had founded the prestigious *Journal of Comparative Neurology*. On board the ship on his return journey, he met the Dutch ambassador to the USA (Mr Van Royen), who later arranged to send the corrected manuscript of the 1936 edition back to the USA by diplomatic pouch.

A course of lectures in Denmark and Sweden (1926) was followed by the invitation of Yale University to accept a doctorate *honoris causa* as well as assume a chair and the directorship of a yet to be built, new Institute of Anatomy. This imminent development, conveyed by C.U. to the Academy and University authorities, promptly exerted its leverage effect: C.U. was appointed Extraordinarius in Amsterdam in 1929. Winkler and Bolk saw to it that Dusser de Barenne obtained a position in New Haven. In September of that year, C.U. was absent again for a series of lectures at the American University in Beirut, using that opportunity to collect craniometric-anthropological data from Phoenician, Arab and Jewish skulls in Syria, Turkey and Palestine. As Dr. J.C. van der Horst – who had acted as C.U.'s *locum tenens* in the Institute during the latter's prolonged absence in 1923/1924 (China) – was unavailable (he had assumed a Senior Lecturership in Zoology at the Witwatersrand University Johannesburg), C.U. found Ernst de Vries (on a holiday from Peking) willing to stand in for him at the Institute. On returning home, C.U. learnt (June 1930) that his closest friend and guardian angel, Prof. L. Bolk, had died.

In the year 1931 he received the distinction of the order of the Dutch Lion. The same year saw him in Scotland (University of Glasgow) for a doctorate *honoris causa*, and in Ireland (University of Dublin) for the John M. Purser lecture and a doctorate *honoris causa*. In 1933 he was in London (Ferrier lecture), in Chicago (doctorate *honoris causa*) as well as New York to exchange thoughts with the renowned anatomists Fred Tilney and Hendry Alsop Riley, and in 1935 in Philadelphia for the Mary Scott Newboll Lecture. At the London Neurological Congress in 1935 he read a long paper on the hypothalamic nuclei, subsequently went to Budapest as representative of both the universities of New Haven and Amsterdam on the occasion of the tri-centenary of Hungary's Pázmány University, and, in 1937 to the USA (membership of the American Academy) and Toronto (Congress of Anatomy). Just before World War II broke out, he attended the third International Congress of Neurology in Copenhagen. Halfway through most attendants left because of the imminent war, much to the disappointment of the president, the distinguished V. Christansen.

During the German occupation, he prolonged the lives of several hundred Jews, preventing their deportation by the S.S. to the gas chambers by providing them with 'scientific' craniometric proofs (in collaboration with the physical anthropologist Prof. A. de Froe) that they were not Jews. Of the ten academics who obtained their Ph.D. degree with C.U. as their promotor, the recently deceased David Moffie was, as the 9th, in 1942, the last Jew to reach this top of the academic Olympus. Shortly after, Moffie was deported to a concentration camp in Poland, which he barely survived, while his young wife, separated from him in another camp, left her life. The son of C.U.'s elder brother, Jan Ariëns Kappers, received the qualification as a doctor/physician from his uncle in 1938 and succeeded C.U. as director of the Central Brain Institute in 1962.

It is remarkable to note that, during C.U.'s long career as director of the Central Brain Institute and as professor of comparative neuroanatomy, the number of theses written under his direction remained restricted to only ten. C.U.'s own scientific production may be characterised as prolific. In this productivity two striking peaks can be distinguished, one between 1910 and 1920, the other between 1930 and 1940. Not all his papers were published in peer-reviewed journals and a number of his articles concern histological techniques or bibliographical matters.

As the librarian of the Netherlands Society of Psychiatry and Neurology he edited two inventories of available journals that were published as such. Being the editor-in-chief of *Folia Neurobiologica* a number of his scientific lectures were published later in this journal by himself. Many of his papers between 1911 and 1922 were published in the *Psychiatrische en Neurologische Bladen* when he was editor-in-chief of the journal. If one considers the large number of collaborators that worked under his aegis over the years within the Brain Institute, it is intriguing that CU almost never published a co-authored article.

Having made a resounding success of the Central Brain Institute, where close to 70 foreign colleagues from all over the world and well over 40 Dutch colleagues did their research during the 37 years of C.U.'s directorship, his own professional scriptorial activity diminished to come to a halt after 1941. He continued his lectures in anatomy in his usual stately and dignified manner – as the Leiden medical historian Prof. Luyendijk-Elshout who attended them told us – up to the closure of the university by the German occupational authorities. After the liberation of the Netherlands he tried, in vain, to prevent the unjustified demission of Prof. Brouwer.

Having spent a holiday in Switzerland in June 1946, where he gave some lectures, he suffered a *mors subita* in the morning of July 28, 1946. With his death, the grand era of comparative neuroanatomy, that knew such men as Cuvier, Edinger, Cajal, Elliot Smith, Judson Herrick, Apathy, Beccari and Boeke, all but ended, the magnificent opus of Prof. Nieuwenhuys (University of Nijmegen) constituting the last manifestation in a once vigorous domain of neuroscience. Wilhelm His's creation of a Brain Commission by joining many national academies in order to establish Institutes of Brain Research each of which was to be charged with research of a certain province of the field of neuroanatomy, now exists for a century. It initially included Amsterdam, Frankfurt am Main, Leipzig, Madrid, St. Petersburg, Vienna, and Zurich. However, only a few of them have survived (amongst them the Cajal Institute in Madrid). Despite its vitality and fame, the Amsterdam Institute, which has been directed by Prof. Swaab since 1978, seems to be threatened with losing its independence as an Academy Institute within the near future for ... economical (??), political (?) or other hilarious motives. C.U. will turn in his grave.

The work

As Van Valkenburg (who left the Institute already after 4 years of deputy-directorship, probably because their personalities were incompatible) pointed out, one can discern three main foci of interest in C.U.'s work: neurobiotaxis, the folding of cerebral and cerebellar cortex, and craniometry.

During his research on the CNS of vertebrates, beginning in 1903, widening in Napoli, and maturing in Frankfurt, C.U. noticed a gradual shift in the location of nucleus VI, nucleus VII, nucleus X (nucleus ambiguus) and nucleus XII in the medulla oblongata of the Ganoids (Teleosts, Selachii, in particular Lophius piscatorius and Lepidosteus) as to their topographical position. This shift *vis-à-vis* each other was striking when he arranged his findings according to the phylogenetic ascendence. In his first publications on this phenomenon he coined the term 'quadrille des noyaux'. In the search for an explanation for this 'dance' of those motor nuclei, the fortunate idea grabbed him to relate the nuclear quadrille to the adjacent (afferent) fibre tracts, providing strong or repeated stimuli to them.

In doing this, he succeeded in showing that the initially ventrally located nucleus VI migrates dorsad to occupy a position near the dorsal longitudinal fascicle subserving the coordinating fibre system, whereas the nucleus VII migrates from a rather dorsal position more ventrad to approach its corticospinal afferent contingent of fibres. Hence, the internal genu of facial fibres, so baffling to the uninitiated. The nucleus XII, initially lying ventrobasally, migrates progressively dorsad during phylogenesis, conspicuously so when fish-genus develop a tongue (gustatory afferents!), whereas the nucleus ambiguus X, the magnocellular part of X that originally has a dorsal position, descends to form another internal genu of its fibres, while the visceromotor parvocellular part retains the initial position. On the basis of associating change in sites of entire nuclei with the afferential input of fibres, C.U. formulated a functional explanation for anatomical topography, in short, a morphological principle of causation. He elaborated this 'law' of the decisive influence of strongest and/ or most frequent stimulation (energy input) in a number of papers between 1907 and 1920.

The second focus of interest aimed at a similar explanation for the cortex development. Wilhelm His Sr. thought that cortical neuronal growth and migration was determined mechanically, i.e., along the direction of least resistance. Others entertained the idea of (re-) generation of axons along preformed paths, such as Schwann-cell tubes for regenerating axons of the proximal stump of a cut nerve. Cajal had voiced the suggestion that, during embryonal neurogenesis, outgrowth and direction of dendrites and axons was determined by trophic substances (repulsive or attractive), but admitted to be at a loss with respect to how to identify these hypothetical entities, as well as confessing to be unable to solve the mystery of the neuronal perikaryon's 'dynamic polarisation' – a mystery that remains unsolved today, but that does not concern us here.

C.U., in his Brain 1921 paper, pointed out that it is not only the cortices that exhibit progressive gyration (and 'sulcation') but that the internal grisea do so too: the cerebellar dentate nucleus, the inferior olivary, the lateral geniculate, the hippocampus, colliculi and the reptilean lamellar nucleus. He advanced the thesis that all this, under the influence of external habitat and life-style of the organism, is caused by functional input factors: the increase in surface (instead of thickness) of the grisea is determined by (the size and/or strength of) afferent input. This is why, in phylogenetic ascendence, the archi- and palaeopallium, originating from the olfactory cortex, are progressively pushed asunder by the neocortex subserving new functions. Ernst de Vries convincingly argued the same distinction to be made within the striatum.

In later years, C.U.'s focus of interest gradually moved to physical neuro-anthropology (brain-casts) and craniometry (skull endocasts and brains), probably influenced by the lessons of L. Bolk and his knowledge of Dubois (Pithecanthropus erectus Java), Professor of Geology in Amsterdam. C.U. collected hundreds of brains and skulls for the Institute's collection during his far- flung voyages from the Mid-East, Far East and North America. He hoped to probe the question whether 'the brain forms its own shell', and to distinguish what (external) factors determine the cranial shape and volume of the many varieties of Homo sapiens since prehistoric times. Many booklets, lectures, and papers of C.U. testify to this, ultimately abortive, exercise.

Finally, his tendency to search for associations and relationships (between form and function, truly Aristotelian! Or between simultaneously activated brain-regions, etc.) led him to consider the parallelism between mind and matter, between psyche en cerebrum. His monograph 'Zielsinzicht en Levensopbouw' [insight into the mind and the structuring of life] betrays a fundamental mixture of protestant-religious upbringing, ethical imperatives, and influences from Spinoza ('Ethica' - the *liberum arbitrium* is an illusion; man is a modus of God; excellence is as difficult as it is rare…) and Bergson ('Elan vital'; 'Matière et Mémoire; l'Evolution créatrice'…), two philosophers which Van Valkenburg and C.U. often discussed between 1909 and 1913. This last focus of interest, being metaphysical, of course is devoid of scientific significance, but is a part of his scriptorial oeuvre and therefore mentioned here.

The person

The reader may have inferred from the preceding text that C.U. was a neuroanatomist obsessed by his profession to the exclusion of the customary foibles to which the average living individual is heir. The dry records are restricted to documented facts. They seem indeed to imply such an image. Those, who wonder what went on behind the façade, will mainly have to revert to (re-) reading the condensed autobiography as the only source of self-revelation. To get a glimpse behind the coulisses one has to read between the lines and look for things unsaid.

C.U. was unquestionably an intellectually brilliant and creative man with an exceptional memory and an exhaustive grasp of pertinent literature. Those who knew and still remember him pointed out his stately bearing, measured gait, benevolent mien, unruffled composure, conciliatory nature and optimistic outlook. On pondering the text of the condensed autobiography, the realisation gradually dawns upon the reader that in this man also dwelt a soul that appears to lack true warmth or deeply-running emotions, a soul tending to narcissism and ambition-inspired calculation (largely unconscious of that of course), inclined to seek out those of influence who hold the potential to promote his goals, and to exploit fellow-men, a soul that essentially remained lonely throughout life. The evidence for such a rather harsh surmise is as tentative as it is tenuous, but it is there if one looks for it.

These days, writing your autobiography is looked upon as narcissistic, as something to be expected from politicians and their likes. Of course, it may be a symptom of insecurity, of self-doubt, or a need for recognition. Certainly, it may have been a vanity acceptable in C.U.'s days, if we recall that Cajal, Von Koelliker, Von Monakow, Forel and Winkler also indulged in the same activity. But is the real need any other than what Narcissus hoped to satisfy by looking at his reflection in the water?

Let us proceed with the explorative exercise. Usually, one makes friends for life during the student years at university. Though C.U. was fortunate in having such friends as Luitzen Brouwer (the world-famous mathematician later on), J.J. van Loghem (bacteriologist), A.J.P. van den Broek (anatomist) and L. le Cosquino de Bussy (zoologist, indologist) among the members of the fraternity 'Dispuut Newton', he does not mention them later. In fact, he does not seem to have developed close friendships in his life, perhaps with the exception of the 10 years older Louis Bolk and the mysterious Cooper (*vide infra*). He studied medicine, but choose a career, which safeguarded him freedom from (emotional) involvement with suffering patients. He scarcely mentions in emotional terms the quality of his relationship with his father, his brothers, and even his mother. He summarily disposes of his relationship to his wife and their marriage in half a page. Taken together, this indicates either a coldness of character, a lack of feeling or ... it betrays a conflict, a battle between the Apollinic and the Dionysian sides of his nature, in which he had decided that the harmonious grace of Apollo should prevail.

Numerous events further seem symptomatic of calculating ambition and exploitation: with inimitable finesse he got Winkler to coach his work for the essay that won him the gold medal; by studying Italian and through contacts made with world-famous Italian experts at the Anthropoly Congress in Amsterdam, he succeeded not only in receiving invitations from the latter but also obtained – an unexplained mystery – a governmental grant to work in Naples, while he was still a student. He persuaded the later anatomist J.B. Johnston to retranslate and correct his M.D. thesis and subsequently sent it to the prestigious *Journal of Comparative Neurology* for publication, where it was accepted.

A telling example of his charming and ruthless *modus operandi* was recalled by Palay (1991) in referring to Herrick's memoirs: A fire in the building which housed Herrick's office, laboratory and all the Journal's records and files, destroyed everything except a fire-proof safe. The latter contained Johnston's translation of C.U.'s text plus the author's footnotes and textual changes, written in blue ink in the margins. On opening the safe, the manuscript proved to be severely charred. Herrick, the dutiful editor, with utmost care, pried loose every leaf and, holding it at a certain angle against the sunlight, transcribed the text and supplied missing or illegible parts of it from his own memory and experience, and typed it out. This final C.U./Johnston/Herrick product was despatched to Amsterdam; it returned, surprisingly, with very few changes. No mention is made of a word of thanks to Herrick who had spent most of his long summer holidays on the job, was nearly 50, and suffered from tuberculosis. Nor is any mention made of the obvious alternative, of C.U. sending a copy of Johnston's translation plus his own annotations to the editor Herrick, which would have saved the latter endless trouble.

He visited Edinger in Frankfurt to give him a copy of the thesis and a report of his work in Naples, which soon led to Edinger's offer of a position in Frankfurt as well as, later on, Edinger's support for the appointment to the Directorate of the Amsterdam Brain Institute. He induced colleagues in the Mid- and Far East and America to collect brains and skulls for his collection and subsequent publications, charmed Elisabeth Crosby into a nine-year lasting translation and update (together with Carl Huber) of his 3-volume work on comparative neuroanatomy, the corrected manuscript of which was expedited safely back by diplomatic pouch through the good offices of the Dutch ambassador to the USA whom he happened to meet aboard the ship on his return and with whom he managed to have daily hours of walking and talking on the deck. His 'good friend', the wealthy honourable Miss J. van Heekeren van Kell, about 30 years his senior, with whom he made numerous trips abroad, was implicitly persuaded to donate a parcel of the land she owned near Loghem for the additional construction of a hall and a number of overnight-stay houses to accommodate the meetings of the 'Woodbrookers' in Barchem, a club of which she and C.U. were members.

Curiously, one looks in vain for signs of hobbies. Apart from having been an avid reader of the books by Jules Verne – which made such a lasting impression on him as a boy that he joined the Jules Verne Society from its start in 1935 (he was 58 years old at that moment) – he was not a literature addict. Neither were sculpture – apart from a brief spate of clay modelling under the guidance of the sculptress R.M. van Dantzig (who later went to Brussels, having sculptured both Winkler's and C.U.'s bust) – nor music, nor painting, nor antique culture foci of his interest.

In his mid-thirties, C.U. – who one would regard as a man of iron logical discipline – displayed symptoms of a baffling irrational slant. He joined the ranks of the anti-alcohol 'Order of Good Templars' (as usual without noticeable social effects) and joined the 'Woodbrookers', a society of ethical, semi-religious, liberal, idealistic, and high-minded people (among them the historian G. van der Leeuw and the poet/writer Henriette Roland Holst). They shared a sincere yearning for God with the ideal to elevate the mental level of the underprivileged working-class as an apparent compensation for their deficient sense of reality testing. The movement resembled such phenomena as the 'Réveil' and the 'Moral Rearmament' ('Caux'). It did not prevent the World War. In the same vein, he visited prisons to read to the inmates. Moreover, C.U., who as a laboratory-man could not have the foggiest notions about the treatment of patients, instigated an association for 'Neurotherapy', the reports of which were published in a special section of the *Psychiatrische en Neurologische Bladen* between 1919 and 1929. The association soon died a taciturn death. All of the above are essentially good intentions on a floating abstract level, remaining as admirable as clearly impotent, subject to Brecht's dictum 'Erst das Fressen und dann die Moral'.

A final remark concerns another aspect. There is not a single indication in either the dry records or the autobiography of even the briefest infatuation, or flings with girls. It looked as though he would remain a bachelor, as his mentor Bolk had been. However, he married after crossing the proverbial threshold of senescence: at the age of 60. One can hardly interpret this as a loud and convincing clarion-call of irresistible heterosexual urges. He married Bea C. van Hunteln, the impressively affluent widow of E.A. Lehmann, who owned a large and stately mansion on the Overtoom in Amsterdam and used to be chauffeured about in her Rolls Royce. The marriage took place a short time after his friend Cooper – to whom (as he emphatically stated) he was very strongly attached during the decades that he, his mother, aunt and family's housekeeper lived in Cooper's house – had died. The marriage remained childless.

The image of the personality which emerges from the sources – and which of course is open to substantial modifications and additions should the present authors have had the time to read the full text of the autobiography and to interview surviving descendants of the family – is one of a unique man, an exquisite neuroscientist, an idealist, of whom (to borrow C.G. Jung's distinction) the beautifully polished Apollinic phenotype served to control and subdue a chthonic Dionysian turmoil of undercurrents, crosscurrents, and counter-currents. Born near the close of the rigid Victorian era, imbibed with protestant and idealistic culture in the *fin de siècle* when – as George Steiner argued – the West was optimistically convinced that it had reached the culmination of civilisation, and entering a century of modern science as well as of the unbelievable barbarism of Lenin, Hitler and two World Wars destroying much of it, his personality may be perceived as one mirroring abysmal conflicts. As such, he was a true child of his time.

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A. Biemond *1902-1973*

17

J.A.M. Frederiks and A.A.M. Blomjous

Figure 1.
Prof. Dr A. Biemond.

Arie Biemond was born on May 5, 1902 in Amsterdam. He lived and worked his entire life in this city. He studied medicine at the Amsterdam University, and qualified as a physician in 1926.

In 1926 he became assistant to Prof. B. Brouwer (1881-1949) who initially had his department of neurology at the Binnengasthuis, later in the Wilhelmina Gasthuis (Pavilion 2) in Amsterdam. The subject of Biemond's M.D. thesis (Amsterdam, 1929) dealt with an experimental and anatomical study of the corticofugal optic connections in the monkey and the rabbit ('Experimenteel-anatomisch onderzoek omtrent de corticofugale optische verbindingen bij aap en konijn'; promotor: Prof. Dr B. Brouwer). In the same year, he became *chef-de-clinique*. During the years of World War II he lectured clandestinely. On May 10, 1943 he had asked, with a number of colleagues, for exemption from his teaching duties.

In 1947 he was appointed professor of neurology at the University of Amsterdam as the successor to Brouwer, a position originally held by J.K.A. Wertheim Salomonson (1864-1922). Biemond's inaugural oration in 1947 dealt with hereditary nervous system diseases ('Enige beschouwingen over erfelijke organische zenuwziekten'). Besides his regular work in the academic clinic, he established a private practice.

Biemond retired on December 31, 1970, because of poor health and impaired vision. In his valedictory lecture (January 30, 1971) he criticised the increasing costs of medicine at the time and gave an explanation of the subjective experience of certain neurological disorders (hemianopia, dysaesthesia). He died in Amsterdam, August 30, 1973, at the age of 71. Prof. Dr. W.A. den Hartog Jager (1913-1993) succeeded him.

Most of Biemond's ± 150 publications in Dutch and international journals are characterised by an explicit foundation of his conscientious clinical observations, usually bolstered by pertinent neuropathological findings. Moreover, he was the author of two unique major textbooks on neurology, based on personal experience. The words 'bedside neurology' run through the two volumes as a continuous thread. One book deals with brain diseases: it was published in 1946, and has been updated and reprinted several times, and translated into English (1970). The other book deals with diseases of the spinal cord and peripheral nervous system. The book on brain diseases is largely based on the author's observations of patients in his clinic and the findings of some 1000 necropsy cases. Unfortunately, his work on an updated edition (and a translation into English) of his book *Spinal Cord and Peripheral Nervous Diseases* could not be completed. For decades both textbooks were standard reading for students at all Dutch universities.

Biemond's name has earned lasting fame through several publications of high quality. He was the first to describe the disturbance in the potassium metabolism (hypokalemia) in familial periodic paralysis. Well-known is his work on the hereditary degeneration of the posterior column. Other areas for which had showed long-continued interest were (experimental) cervical position nystagmus, spinocerebellar degeneration, Guillain-Barré syndrome, ataxia telangiectasia, poliomyelitis anterior chronica, and contusio cervicalis posterior.

Several of his *princepes* papers won eponymic recogniton:

- Biemond's disease (also called Biemond syndrome I, Biemond's ataxia, or posterior column ataxia) stands for hereditary posterior column ataxia. The ataxia is due to degeneration of the posterior column and large fibres of the dorsal roots, and loss of Purkinje cells. Transmission occurs as an autosomal dominant trait.
- Biemond's hypothalamic syndrome (also called Biemond syndrome II, Biemond-Van Bogaert syndrome) defines the clinical entity of the Bardel-Biedl syndrome combined with iris colobomas. The syndrome is characterised by mental retardation, coloboma of the iris, obesity, hypogonadism, and polydactyly. Hypospadia and hydrocephalus may occur. The syndrome is believed to be transmitted as an autosomal recessive trait.
- Congenital familial analgesia, Biemond type. This form of congenital insensitivity to pain is characterised by an absence of pain sensation, diminished touch and temperature senses, and absent tendon reflexes. The pathological findings showed defects in the posterior root ganglia, Gasserian ganglion, posterior roots, posterior horns, posterior columns, and the spinal grey matter. Transmission occurs as an autosomal recessive trait.
- Myopathia distalis juvenilis hereditaria. The relatively benign disorder is characterised by symmetrical paresis and atrophy of the distal muscles of the extremities. The onset is between the ages of 5 to 15 years, progression occurs up to the age of 50 years, when it becomes stationary. This familial syndrome is transmitted as an autosomal dominant trait.
- Brachydactyly-nystagmus-cerebellar ataxia syndrome. This syndrome consists of brachydactyly (shortening of the 4th metacarpal bone), cerebellar ataxia, nystagmus, strabismus, and mental retardation. The condition is believed to be transmitted as an autosomal dominant trait.

His superior knowledge of neurology (rooted in a vast knowledge of the literature and vast personal clinical experience), combined with his tact to guide his staff, his great zest for work, and his constant, enthusiastic dealing with neurological problems, made him a unique and gifted teacher. He liked to examine and demonstrate a patient and to walk the wards. His scrupulously careful way of examining every

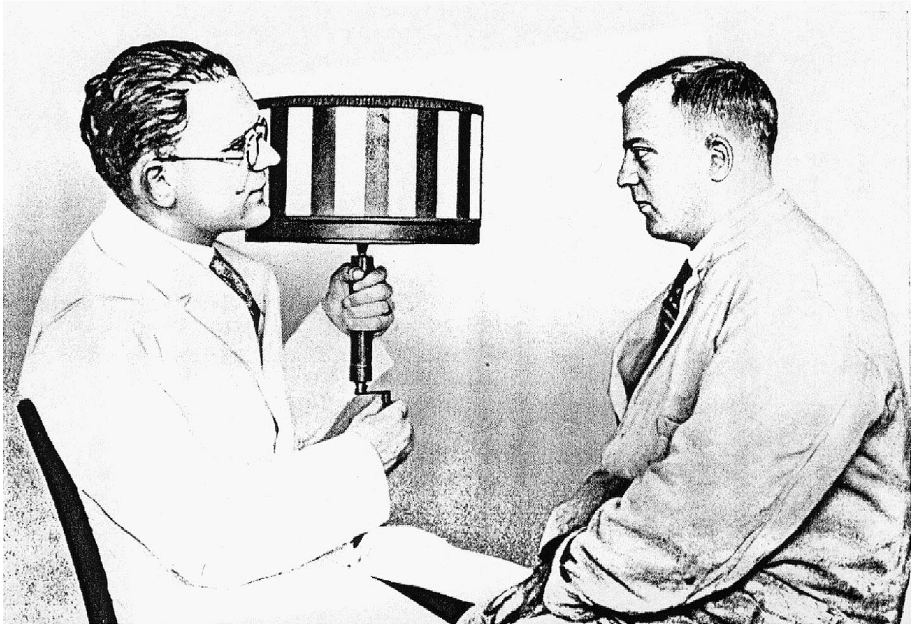

Figure 2.
Examination of the optokinetic nystagmus.

patient was legendary in students and staff circles. He enjoyed teaching at the bedside and in the lecture hall. Many of the students judged his lectures as the best in the medical faculty in Amsterdam. Biemond prepared them meticulously. The present authors, both trainees of Biemond, can only testify to the veracity of these statements.

Biemond repeatedly pointed out to his disciples the overriding significance of clinical symptoms and signs. In diagnostic considerations, he said, they always have to come first in any relation with laboratory findings and other diagnostic technical tests. In the preface to the book *Brain Diseases* this fundamental clinical attitude is unequivocally formulated: "We are living in an era in which the, admittedly indispensable, 'mechanical' diagnosis of brain diseases by means of pneumoencephalography, arteriography, electroencephalography, echoencephalography, scintigraphy, etc., threatens to undermine the importance of clinical investigation." In the opinion of the present authors, this warning in principle still holds true.

Biemond supervised the doctorate theses of 30 disciples, among whom one of the present authors (JF) graduated on the body scheme and its disorders.

After World War II, Biemond stimulated several of his staff members to specialise in sub-specialities, such as neuropathology and muscle diseases (J. Bethlem), paediatric neurology (P. Fleury), neurological intensive care (L. van Trotsenburg), neuroradiology (H.W. Stenvers, Jr), electromyography and electroencephalography (W.J.M. Hootsmans) and experimental neurology (W.A. den Hartog Jager). Neurosurgery, introduced in the Netherlands by Brouwer (1929), also had its residence in Pavilion II of the Wilhelmina Gasthuis (Prof. Dr W. Noordenbos). This continued the close collaboration of the two clinics, established by Brouwer in 1929.

In short, Biemond set up the best neurological academic clinic in the Netherlands, which also had an excellent reputation abroad: "Amsterdam is not only the capital of the country, it has from the very beginning been the centre of Netherlands neurological science" (Biemond 1959). He would have been pleased to read some 20 years later (had he lived long enough): "Most of the neurologists now practising in the Netherlands are scientific descendants in the first, second, or even third generation of the Amsterdam neurological school" (Schulte and Endtz 1977).

Like most neurologists of his generation, Biemond did his own neuropathological work-up and diagnosis. He was one of the early members of the Section of Neuropathology, founded within the Netherlands Society of Psychiatry and Neurology.

Biemond was active in, and twice president of, the Society of Amsterdam Neurologists. This Society played a leading role in Dutch neurology for many years; it was founded in 1909 by fourteen Amsterdam neurologists among whom figured internationally renowned names such as Ariëns Kappers, Bolk, Van Valkenburg, E. de Vries, Wertheim Salomonson and Winkler. In 1959, on the occasion of the 50th anniversary of the Society of Amsterdam Neurologists, Biemond edited the memorial volume: 'Recent Neurological Research'.

Biemond was scientific supervisor of the Alexander van der Leeuwkliniek in Amsterdam, a hospice for epilepsy, during the 1960s. Later, this clinic became associated with his neurological clinic at the Wilhelmina Gasthuis, and thus lost its categorical character.

Biemond was Chief Editor of the Psychiatric and Neurological Papers (*Psychiatrische en Neurologische Bladen*) from 1941 until 1949. From the beginning in 1964, he was a member of the editorial board of the multivolume *Handbook of Clinical Neurology*, edited by P.J. Vinken en G.W. Bruyn, and acted as editor of Volume 2, 'Localisation in Clinical Neurology' (1969).

It is no sinecure to sketch Biemond's personality. In any situation he left the indelible impression of a man with a strong and honourable character. The subject of his conversations usually concerned neurological problems, which he invariably discussed with great enthusiasm. In fact, he considered neurology as "the queen of specialities" (Biemond 1959). More than once, he surprised his pupils with a vast command of the neurological literature. Every day, at the customary 'morning statement', he gave his disciples a selection of the literature he had read the evening before ("I have read for you...").

As an individual he was hardly known, even to his staff members. He was punctual in his manners and dress, was even tempered, and rarely divulged things of his private life. Occasionally, he showed his inclination to history and French literature. It was for this reason, therefore, that he was greatly pleased when one of the present authors (AB) as a young pupil, used the term 'sclérose en plaques' instead of the common term 'multiple sclerosis' in one of his first case histories. Equally occasionally, he let on that he was interested in Amsterdam's football club Ajax. See also Voorhoeve (in press).

In 1940, the Ramaer Medal of the Netherlands Society of Psychiatry and Neurology was awarded to him. J.N. Ramaer (1817-1887) was one of the founders of The Netherlands Society Psychiatry and Neurology. On that occasion, the usual laudation emphasised Biemond's exactitude in research and his talent in combining clinical-neurological data with neuroanatomical and neuropathological findings.

Biemond was honorary member of the 'Société Française de Neurologie', the 'American Neurological Association', the 'Society of Amsterdam Neurologists ', and the 'Netherlands Society of Psychiatry and Neurology'. In 1971, he was honoured by the high royal distinction of 'Knight in the order of the Dutch Lion'.

On the occasion of his retirement on January 30, 1971, a bust of Biemond was unveiled in the auditorium of the University of Amsterdam, and on the site of the former Wilhelmina Gasthuis, one of the new streets has been named 'Arie Biemond straat'.

The refresher courses of the Netherlands Society of Neurology for its members have been called 'Biemond courses' since 1999. Biemond's name will continue to be a living example for present and future generations of Dutch neurologists.

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L. Bolk *1866-1930* 18

D. Moffie †*

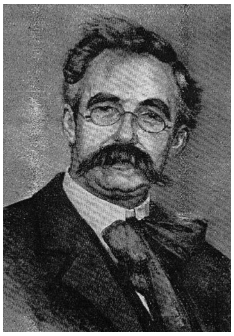

Figure 1.
Lodewijk Bolk

Louis (officially Lodewijk) Bolk was born on December 10, 1866 in Overschie, a village near Rotterdam. After primary school, he visited the gymnasium, but left before the final examination, without a diploma. In 1885 he began working in the office of a notary public in Waalwijk, a small provincial town, and in 1888 he passed his baccalaureate examination. However, he was not satisfied with this work, as he felt more attracted to medicine.

He enrolled to study medicine in 1888 at the University of Amsterdam and he passed the baccalaureate examination three years later. As a student he was awarded the gold medal in 1892 for a prize-winning investigation on the origin and peripheral distribution of the nerves in the human lower extremity. As a medical student, Bolk already published some important papers on innervation of the skin and segmentation (1894, 1895). In 1896 he passed his final examination as a doctor of medicine. He became assistant to the German anatomist Professor Georg Ruge (1852-1919) in 1897, however, Professor Ruge left Amsterdam the very same year because he had accepted a nomination at the University of Zürich. Ruge had proposed his prosector and nephew, Dr. O. Seydel, also a German, as his successor. This aroused opposition in the Municipal Council of Amsterdam which had the right of nomination; Ruge's predecessor, Max Fürbringer (1846-1920), Professor of Anatomy from 1879-1888, had also been German and both had left Amsterdam earlier than had been agreed for nominations elsewhere. The younger professors of the faculty, too, felt that it was high time to nominate a fellow-countryman, if only to lessen this risk.

One of the persons interested in this vacancy was Eugène Dubois (1858-1940), pupil of Fürbringer and (after his medical study) his prosector. In 1886, Dubois became lector in human anatomy with a good chance of becoming Fürbringer's successor. However, after a disagreement with Fürbringer, Dubois took his leave. He went to the Dutch East Indies as a military doctor in 1887. There he made his famous discovery of fossil bones of 'the missing link', which he called the Pithecanthropus erectus, which earned him the honour of doctor *honoris causa* of the Amsterdam University in 1897. However, he did not get sufficient support for his (half-hearted) efforts for the chair of anatomy. Instead, he was appointed Professor of Geology at the University of Amsterdam, in 1898, probably as an ointment for his hurt feelings (Shipman 2001).

After some lobbying actions by the students, a fierce paper war in the daily newspapers and in *Propria Cures*, the proposed short-list of candidates was discarded and Bolk, aged 39, who had figured second on the list, was nominated. He held the inaugural lecture 'De morphotische eenheden van het menschelijk lichaam' [The morphotic entities of the human body] on May 2, 1898. In this lecture, Bolk, in a rather philosophical manner, unfolded his ideas about evolution and the planning of his own future work. He praised Ruge's scientific spirit, but did not waste a single word on their human and social relationship.

In the second half of the 19th century and the beginning of the 20th century, segmental anatomy, which had its origin in older theories of metamery (Lubosch 1925), was a focus of interest of many anatomists, physiologists and clinicians (van Rijnberk 1908, Hansen and Schliack 1962). Experimental work had been done by Sherrington (1893, 1898) on monkeys to elucidate the radicular innervation of the skin (dermatomes) and muscles (myotomes).

Bolk used the dissection method to follow the root-fibres from the brachial and lumbosacral plexus to their periphery, unravelling the composition of the plexus, delimiting dermatomes and myotomes. With this method, it was only possible to follow the fine fibres of the dorsal root to the subcutis. Therefore, Bolk's dermatomes are smaller than those established by Sherrington, because with Bolk's method the 'overlap' is less conspicuous, which is, in fact, an advantage in clinical practice.

From observations of the cutaneous eruptions of herpes zoster, a chart of dermatomes was composed by Head and Campbell (1900), which were similar to those after dorsal root section to alleviate spasticity and pain (Foerster 1936).

Bolk's *Das Cerebellum der Säugetiere* [The cerebellum of mammals] (1906) was composed of three papers on the comparative anatomy of the cerebellum, published earlier in a new anatomical journal, *Petrus Camper*, founded by Bolk and Winkler in 1902. The journal appeared for only a few years. In this monograph, Bolk presented a new subdivision of the cerebellar lobi and lobuli and attempted to correlate their size with the functions of muscle groups. This relationship of form and function led him to the idea of a somatotopy in the cerebellar cortex, such as was known for the Rolandic area.

Bolk's division of the cerebellum and his ideas on localisation were accepted by Winkler, who described them in detail in his *Handboek der Neurologie* (1926).

These ingenious but speculative conclusions on cortical cerebellar localisation were based solely on embryological and comparative anatomical data. Nowadays they are mainly of historical interest (Clarke and O'Malley 1968, Finger 1994).

Bolk's ideas gave an impetus to new research of the cerebellum (Larsell 1937, Larsell and Jansen 1972) and also to much criticism from physiologists and clinicians. "My observations consequently lend no support to a circumscribed or focal representation of different portions of the body in the cortex of the cerebellum etc." (Gordon Holmes 1922, 1938).

Electrophysiological experiments in the last decades have refuted most of Bolk's ideas on somatotopy, though in some experiments a certain somatotopy in the cerebellar cortex and nuclei has been found, homolaterally as well as heterolaterally and even bilaterally, on afferent and efferent stimuli (Dow and Moruzzi 1958, Brodal 1981, Groenewegen et al. 1979, Glickstein and Voogd 1995).

Bolk received a second doctor *honoris causa* distinction and, moreover, was offered the vacant chair of anatomy by the University of Leiden in 1905. This offer induced the University of Amsterdam to accelerate the building of a new laboratory for anatomy and embryology, which had been promised to Bolk earlier; in this way Bolk was persuaded to stay at the Amsterdam University. The Central Institute of Brain Research was built at the rear side of the laboratory and was opened on June 8, 1909. Dr. C.U. Ariëns Kappers was its first director and Dr. C.T. van Valkenburg, the vice-director.

Winkler and Bolk had instigated the building of the Brain Institute; they represented the Dutch branch of the International Brain Commission, which aimed at creating central institutes for brain research, in its broadest sense, all over the world or to link up with already existing neurological institutes.

In the same year, the Society of Amsterdam Neurologists was founded (June 13); an initiative of Van London, Ariëns Kappers and Van Valkenburg. Bolk was also one of the founding fathers (Winkler 1947).

After his work on the cerebellum, Bolk became interested in odontology, an interest he maintained to the end of his life, and which resulted in a series of papers. Close to his anatomical institute, a cemetery was cleared and all the exhumed material, skeletons, skulls, teeth etc., was taken to the institute and furthered his interest in physical anthropology. He also investigated the teeth of other primates, mammals and reptiles. The results led him to postulate the so-called 'Dimer-theory', which proposed that the teeth of mammals, especially in primates, were originally composed of two components that had melted together.

In later years, Bolk occupied himself with and work on the evolution of man. As Rector Magnificus of the Amsterdam University (1917-1918), he read a lecture on January 8, 1918 (on the anniversary of the university), with the title 'Brain and Culture'. In an extended form, this lecture was presented in 1926 to the German Anatomical Society in Freiburg with the title 'Das Problem der Menschwerdung' (The Problem of Human Evolution). In adult form, the human body retains some fetal characteristics, which are also seen in the foetus of the chimpanzee. However, in this primate, these features are only temporary and are no longer present in the adult chimpanzee. Bolk called the process of retaining these foetal features in man 'foetalisation'. One example of this is hairlessness, seen in the foetal stage of man and chimpanzee and also in the adult state of man. However, the adult chimpanzee's body is covered with hair. Another example is the place of the foramen magnum in relation to the skull and other features of the skull. The foetalisation theory implies the principle of retardation in the development of man. As a consequence, the different stages of life are prolonged.

In Bolk's evolution theory the principle of foetalisation of the form is a necessary consequence of the retardation in the development of the form: "evolution is not a result but a principle." A similar view is encountered in later works of Dubois (Pat Shipman 2001), who was not a friend of Bolk.

Bolk's ideas have been largely forgotten and are rarely mentioned in textbooks. Keith (1948), who was a friend of Bolk, wrote an essay 'Foetalisation as a factor in human evolution', which contains the essence of Bolk's ideas.

The principle of foetalisation holds true for some somatic characteristics, but not for its link with the endocrine system (Kloek 1941). Nor can it be reconciled with the development of the brain in man (weight, cortical surface) compared to that of the chimpanzee (Changeux 1986).

Bolk was a prolific writer; he wrote about many aspects of physical anthropology, congenital malformations, anatomy of primates, etc., and he may be considered the greatest Dutch anatomist since Petrus Camper (Ariëns Kappers 2001). Several of his pupils occupied the chairs of anatomy at Dutch universities.

For the neurologist and neuroscientist, his most significant work is in the field of segmental anatomy, the cerebellum, the brain of primates, but also in his ideas about human evolution.

Bolk was painted by the Amsterdam artist Lizzy Ansingh (fig. 1), and later, in 1925, by Monnickendam in the classical Dutch setting of an anatomical lecture (see p. 138 chapter 8). He is surrounded by three of his former pupils, Professors Boeke at the right side of Bolk, Professor v.d. Broek on his left side and Prof. Barge standing (Baljet 1993).

Bolk never married; he was busy being a workaholic. The last years of his life were difficult and tragic. In 1918 his right leg had to be exarticulated on account of femoral osteosarcoma. Between 1918 and 1930 two operations for recurrences of the tumour were necessary. He died in 1930.

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Note

* Dr D. Moffie died on November 16, 2001. J.A.M. Frederiks executed the final editing of the complete manuscript.

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A complete list of Bolk's publications may be found in the obituary by Prof. A.J.P. v.d. Broek: Morphologisches Jahrbuch (1931) 497-516.

B. Brouwer *1881-1949* 19

G.W. Bruyn and P.J. Koehler

Figure 1.
Bernard Brouwer.

Bernardus Brouwer* (23 March 1881 – 1 November 1949, Fig. 1) was born, lived, worked and died in Amsterdam. Originating from a middle class Protestant family (his father, Jan Brouwer, was a local estate agent), he attended the Gymnasium (alpha), studied medicine and, to broaden his views and to follow his inclination to know more about the nervous system, he then went to Zurich, working in C. von Monakow's laboratory for neuroanatomy for a period of three or four months. The 1st International Congress of Psychiatry, Neurology, Psychology & Care for Lunatics (2-7 September 1907), presided by G. Jelgersma (1859-1942) from Leiden, a congress attended by 800 participants, and at which A. Pick, O. Vogt, C. von Monakow, O.L. Binswanger and E.J.R. Ewald, among others, read papers, must have strengthened his resolve to specialise in neurology. The Medical Historical Institute in Zurich holds eight of the letters Brouwer wrote to Von Monakow between 1916 and 1926; these testify to the friendship that had arisen between the master and the pupil despite a 30-year difference in age.

He then became assistant to J.A.K. Wertheim Salomonson (1864-1922; e.o. Professor of Neurology, Electrotherapy and Radiology) and C. Winkler (1855-1941), having been urged by these two to return to Amsterdam. His MD thesis *Deaf-mutism and acoustic tracts*, prepared under the guidance of Winkler, won him the doctor's degree *cum laude* [with honours]on March 12, 1909. In his spare time, he was a highly appreciated football referee and developed his marked talent for music. Later in life, he enjoyed playing golf. Besides assisting Wertheim Salomonson and studying neuroanatomy, Brouwer established a private practice. He married a paediatrician, Hélène Marie Frommann (born in Leiden on 30 November 1883) on 5 November 1909. They had no children.

In 1913 he assumed the vice-chairmanship of the Central Institute for Brain Research, headed by C.U. Ariëns Kappers. The abundant material in this institute quickened Brouwer's scientific mind. Focussing on the comparative anatomy of the cerebellum he soon showed, in accordance with Edinger's concept (then prevalent), that phylogenetically young systems are prone to be selectively affected by certain pathological processes and that the rostral part of the inferior olive is linked to the archicerebellum. Not only Edinger's distinction between archi- (in lower animals) and neo- (in higher animals) cerebellum had inspired him, but also the classic studies by L. Bolk (1866-1930) on the mammalian cerebellum.

Together with the ophthalmologist, Prof. W.P.C. Zeeman (1879-1960), he next studied the projection of retinal fibres to the lateral geniculate body and occipital cortex in a series of rabbits, cats, and monkeys, by producing retinal quadrantal lesions and cortex-ablations (Brouwer and Zeeman 1926). This work was incited by his prediction of the site of the causative lesion in a patient with bilateral hemianopsia, proven correct on autopsy a year later (Brouwer 1915). At the time, a rather vehement international controversy prevailed with respect to the retinal, and specifically the macular projection on the cortex: Salomon E. Henschen (1847-1920, Swedish neuropathologist) asserted the hypothesis of a fixed, restricted, macular representation in the striate cortex ('the cortical retina'), whereas Constantin von Monakow (1853-1930) claimed, on the basis of the clinical fact of macular sparing and of cortical plasticity, that central vision appeared rather widely represented in the occipital cortex, even beyond the area striata.

The Brouwer-Zeeman experiments established the retinal topography in the lateral geniculate as well as a wide, but localised, macular projection on the striate cortex (1917, 1932). They also found a striato-geniculate feedback projection, which Brouwer hypothesised to be the matrix of attention; he synthesised his views in a large monograph (Brouwer 1928). Gordon Holmes' findings in wounded soldiers confirmed their results.

While at all this, Brouwer also analysed the topographical relationship of the various oculomotor subnuclei (Brouwer 1918), which earned him ephemeral eponymous fame ('Brouwer's scheme'), though his conclusions were proven partly erroneous by later work. Brouwer showed that Perlia's nucleus is the nucleus for ocular convergence. Also, he experimentally confirmed Fabritius' findings on the spinal conducting pathways of sensation.

In the meantime, his teacher Winkler returned to the chair in Utrecht (1916-25), ultimately to succeed K. Heibronner (1869-1914) who had died abruptly from a cardiac infarction at a young age. Winkler (Utrecht) and his best pupil, Brouwer (Amsterdam), were now the two leading neurologists in the country with Leiden's Jelgersma, Professor of Psychiatry and Neurology (1899) coming *ex aequo*. When Winkler, a strong driving force behind the Society of Amsterdam Neurologists, left for Utrecht in 1915, Brouwer became the activating principle of this club, acting as secretary and reading 30 papers in the course of the years (Heidema 1934, Winkler 1934).

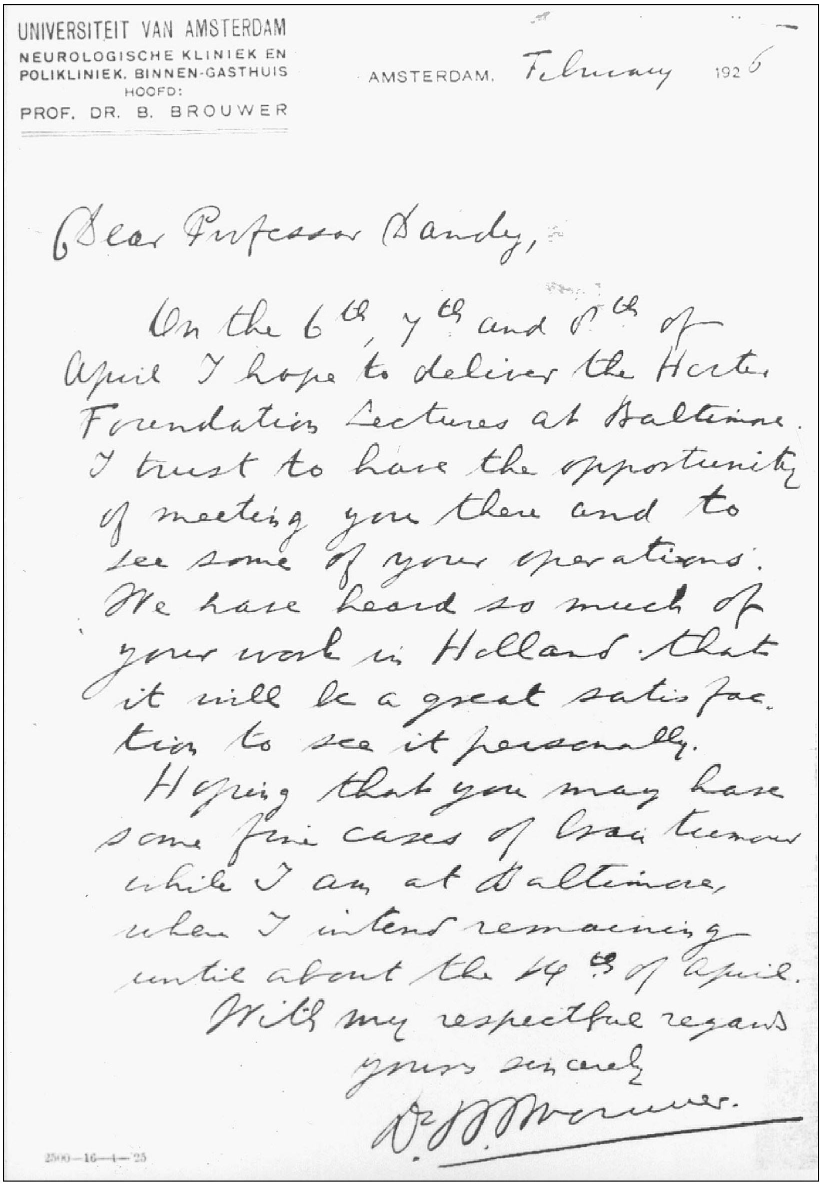
Brouwer, incited by the work of Henry Head (1861-1940) and Louis Bolk (1866-1930) on segmental sensory innervation as well as by personal observation of segmental deficit in syringomyelia manifesting after spinal trauma, tackled this problem by means of material available in the Institute for Brain Research. In the course of these studies, he pointed out the progressive increase in size of the posterior columns through the phylogenetic ascendance, stressed their mediating role in gnostic sensation as well as their vulnerability to pathogenic agents because of their 'recent' development. Meanwhile, he continued to carry out his clinical duties in the Department of Neurology, where Karel H. Bouman (1874-1947) had been appointed to succeed Winkler in the chair (1916). Brouwer did not stand a chance because the assistants found him too interested in 'basics' and less clinically oriented.

Brouwer ultimately succeeded in Wertheim Salomonson's chair on May 28, 1923 with an inaugural address 'On the autonomic nervous systems and emotions'. Together with Leendert Bouman (1869-1936), Professor of Psychiatry at Amsterdam's Vrije Universiteit (who later succeeded Winkler in Utrecht, 1925), Brouwer wrote a 4-volume Dutch *Textbook of Nervous Diseases* (1922-1930) the standard of which did not quite meet his own expectations (Brouwer and Bouman 1922-1930). He was an inspired teacher for the students.

The Johns Hopkins University invited him to read the 17th annual series of the Herter lectures (Brouwer 1926-1927). The invitation was obviously meant as a means of making personal acquaintance, because Brouwer had been invited by the Johns Hopkins to assume a research-professorate in Neurology in Baltimore. The complete staff of the neurological department saw the Brouwers off at Amsterdam's Central Station; the couple would proceed by a ship of the Holland-America line. This might be interpreted as a formal homage, typical of those times, but also, no less, as a sign of the appreciation, indeed, the affection his disciples and collaborators harboured for their boss, a six feet three inches large man with an uncomplicated nature, straight intentions, sovereign sense of duty, purity of heart, a quasi childlike simplicity in social intercourse, and paternal warmth. Brouwer read the series on 6-8 April 1926, but his strong emotional ties with Amsterdam (at which his inaugural address already hinted) made him decline the offer of an Ordinariate at Baltimore. "By coincidence, following my lectures in Baltimore, they offered me a Chair at Johns Hopkins University, in which case I would have the opportunity to design a clinic. Following some discussions with the faculty I withdrew, as I did not want to leave my country" (Brouwer 1946). He reported on his experiences during his 2 months trip through the USA at the October 1926 meeting of the Society of Amsterdam Neurologists (Brouwer 1926, Koehler and Bruyn 2001).

Brouwer was impressed by the *avant-garde* work and high quality of the American neurosurgeons in Baltimore, Philadelphia, Boston and the Mayo Clinics. He met all the protagonists, such as Ayer, Cushing, Frazier, Halsted and Spiller. As evidenced by Brouwer's letter to Dandy (February 1926) he wanted to see the strong interest he fostered for neurosurgery (which he felt to be a new therapeutically promising domain) vindicated by personally witnessing the activities of American neurosurgeons (fig. 2). Convinced by their methods and results, he returned to Amsterdam with the firm resolve to put neurosurgery on its own, autonomous footing as a separate speciality. Indeed, when the newly built neurological department of the Wilhelmina Gasthuis was inaugurated in September 1929, the complex boasted the first neurosurgical university department in the Netherlands. At the occasion, Brouwer read the lecture 'On the future of neurology', a testimony of his convictions (Brouwer 1929). Brouwer had insisted on having an American-trained neurosurgeon at his side, and Ignaz Oljenick (1888-1981; Cushing-trained) became his neurosurgeon. It should be pointed out here, that Brouwer remained chairman of both departments and that it took quite a few years before the neurosurgery clinic acquired the official status of a fully autonomous discipline with a chair. He convinced the municipal authorities of

Amsterdam of neurosurgery's emancipation with the aid of letters to that effect that he had solicited (and obtained) from Cushing, Jelliffe, Nonne, Pette, van Bogaert, etc. Brouwer can rightly be regarded as the founder of neurosurgery in the Netherlands. True to his love, he, together with Verbeek from Groningen, was also co-founder of the 'Neurosurgical Study Circle' seven years later (1936).



UNIVERSITEIT VAN AMSTERDAM
NEUROLOGISCHE KLINIEK EN
POLIKLINIEK. BINNEN-GASTHUIS
HOOFD:
PROF. DR. B. BROUWER

AMSTERDAM, February 1926

Dear Professor Dandy,

On the 6th, 7th and 8th of April I hope to deliver the Herter Foundation Lectures at Baltimore. I trust to have the opportunity of meeting you there and to see some of your operations. We have heard so much of your work in Holland that it will be a great satisfaction to see it personally.

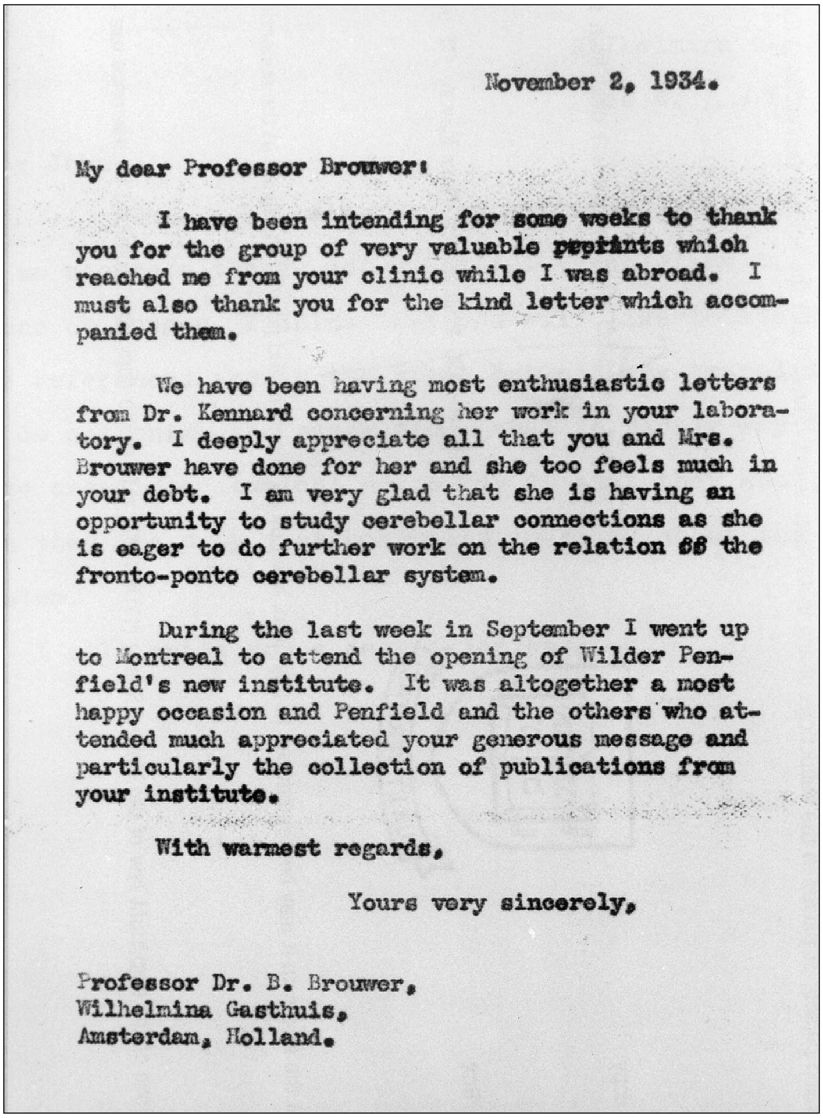
Hoping that you may have some fine cases of brain tumour while I am at Baltimore, where I intend remaining until about the 14th of April.

With my respectful regards
yours sincerely
Dr B. Brouwer.

2500—16—4—25

Figure 2.
Letter from Brouwer to Walter Dandy (February 1926; by courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institution).

Meanwhile Brouwer made a second lecture tour in the United States in 1933. It was at the invitation of the Association for Research in Nervous and Mental Disease in New York (1933). During this tour, he also accepted invitations to visit Yale University, meeting there compatriot Dusser de Barenne (professor of physiology), Boston (Society for Nervous and Mental disease), and McGill University, Montreal. He met John Fulton (1899-1960) at Yale and continued corresponding with him (Figure 3). The connection also resulted in the bilateral exchange of students (Koehler 2001).



November 2, 1934.

My dear Professor Brouwer:

I have been intending for some weeks to thank you for the group of very valuable reprints which reached me from your clinic while I was abroad. I must also thank you for the kind letter which accompanied them.

We have been having most enthusiastic letters from Dr. Kennard concerning her work in your laboratory. I deeply appreciate all that you and Mrs. Brouwer have done for her and she too feels much in your debt. I am very glad that she is having an opportunity to study cerebellar connections as she is eager to do further work on the relation of the fronto-ponto cerebellar system.

During the last week in September I went up to Montreal to attend the opening of Wilder Penfield's new institute. It was altogether a most happy occasion and Penfield and the others who attended much appreciated your generous message and particularly the collection of publications from your institute.

With warmest regards,

Yours very sincerely,

Professor Dr. B. Brouwer,
Wilhelmina Gasthuis,
Amsterdam, Holland.

Figure 3.
Letter from John Fulton to Brouwer (November 2, 1934; courtesy Manuscript and Archives, Yale University Library, New Haven, CT; Fulton, 1934).

After the USA trip, Brouwer more than ever disapproved of neurologists who themselves wielded the trepan and the knife, even in the case of Ludwig Puussepp (1875-1942), for whom he wrote a paper in honour in his Festschrift(Brouwer 1935), or of giant Otfrid Foerster, who, as an internationally known neurologist, decided to devote the rest of his life to practice neurosurgery at the age of forty. This may well explain why, under Brouwer's influence, the life of the highly talented L.J.J. Muskens (1872-1937), lecturer in neurology, author of two hefty monographs on epilepsy and on the supravestibular systems, was not made easy in the neurological circles of Amsterdam. Brouwer considered the neurologist's task to be the exact localisation of the lesion, and the neurosurgeon's to remove it, two domains so complex as to be impossibly combined within the capabilities of a single individual.

His clinical and clinical-anatomical work won recognition in widening circles; it attracted teamwork with, e.g., Prof. C. Cornelia de Lange and Prof. Adriaan G.H.A. de Kleijn (1883-1949). The Netherlands Society of Psychiatry and Neurology conferred the Ramaer-medal upon him (1920); the Royal Academy of Sciences elected him as member (1926); Queen Wilhelmina bestowed the distinction of 'Knight in the Order of the Dutch Lion' upon him. He was elected Honorary Fellow of the Royal Society of Medicine (London, 1936), honorary member of the Harvey Society New York as well as of the American Association of Neuropathology, the Medical Society of St. Louis, the Societas Medicorum Sveranae, the Esthonian and Hungarian Medical societies, and the Society of Amsterdam Neurologists.

Brouwer went to visit his English colleagues on various occasions, reading papers (e.g., The liver, the spleen, and the brain for the Royal Society of Medicine, 1936), and on the clinicopathological findings in a large personal series of cases of hypothalamic lesions. A fairly close friendship arose between Sir Gordon Holmes and Brouwer; they shared quite a few character-traits, such as directness of approach (occasionally erring on the side of bluntness), intransigent honesty in matters scientific and personal, tenacity, indefatigability, energy, disciplined thought balanced by a basically good-nature, and an intrinsically humane attitude.

Thanks to Mrs. Eileen Macdonald Critchley, who was kind enough as to search through the notes and papers of her late husband, the close bond between Sir Gordon Holmes and Brouwer finds confirmation in script (Critchley 1979). In addition, documentation was found concerning various trips Macdonald Critchley made to Amsterdam where he visited Brouwer and Frits Grewel (1898-1973; pediatric neuropsychiatrist), dining at their homes in 1936 (Macdonald Critchley 1990). Mrs. Critchley also dug up Brouwer's affirmative reply of January 6th, 1936 to the invitation by Sir Charles P. Symonds to assist at a dinner of, as well as present a lecture to, the Hexagon Club in Pagani's Restaurant (Critchley 1986). The evening preceding this, Macdonald Critchley met Brouwer and took him to dinner at Kettner's Restaurant. Brouwer´s anglophilic orientation is evidenced by his telltale membership of the 'Medical Pilgrims Club'. At one of the dinners of this club, one notes the presence of Isidore Snapper (1889-1973; Internal Medicine; went to Peking in 1938 and USA in 1941), of Brouwer and 'his' neurosurgeon Oljenick. Bergmann from Berlin was also present, as was the master of medicine Sir Arthur F. Hurst (1879-1944) (Figure 4).

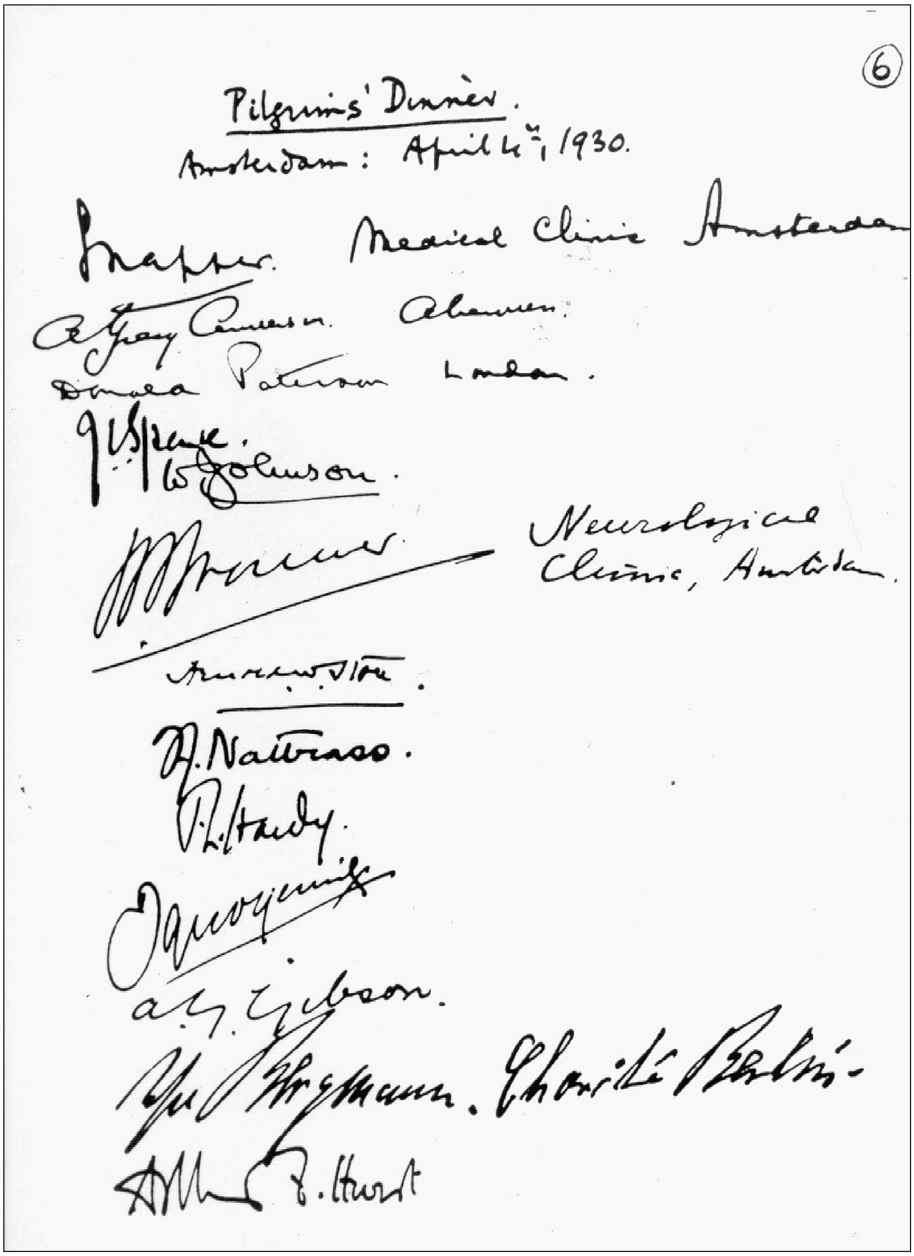

Pilgrims' Dinner.
Amsterdam: April 4th, 1930.
Snapper. Medical Clinic Amsterdam
Donald Paterson London.
W. Johnson.
Neurological Clinic, Amsterdam.
A. G. Gibson.
Charité Berlin

Figure 4.
Participants at the Pilgrim's Dinner, Amsterdam, 4 April 1930, including Snapper, Brouwer, Oljenick, Bergmann and Hurst.

Curiously, when Max Bielschowsky (1869-1940) fled from Germany because of Nazi-persecution to the laboratory in Brouwer's clinic, where a place had been provided for him, the two did not appear to get along well. Bielschowsky found the ambience rather stern and forbidding and, by intermediary of Prof. L. Bouman, his staunch supporter, moved to the laboratory of the Neurological and Psychiatric University Clinic in Utrecht, where he worked until he and his family finally fled to England, the country that very soon was to house his ashes. The tension between Bielschowsky and Brouwer is difficult to explain in retrospect. Perhaps Bielschowsky's behaviour had changed after his first stroke in 1937; Brouwer was of a conciliatory rather than antagonistic disposition, even if his sense of responsibility might generate an internal state of conflict or a divided mind. His patients loved him for his warm and cheerful personality; at home, his deep-running emotions came to the surface in his virtuoso-talent for music.

Brouwer's clinical mind never rested although it appeared to do so. That was the overriding patience of the hunter: in his late sixties he published a milestone paper on subacute cortical cerebellar degeneration due to remote cancer, the first case of which he had seen (and interpreted as due to a toxic agent) 28 years earlier (Brouwer 1919, 1947). His list of papers, as compiled by Biemond (1950) runs to 240. During the war years, he served as president of the Netherlands Society of Psychiatry and Neurology (1939-1943).

A shadow was cast over Brouwer's ultimate years. Whether because of a curious lapse of judgement or because of a constitutional naiveté surprising in a man of his stature and age, but most probably because of his deep sense of obligation and responsibility vis-à-vis the university he served, he assumed the position of Rector Magnificus of the University of Amsterdam during the German occupation. He read the rectorial addresses at the university's anniversary dates in 1941 and 1942. Soon, the occupational authorities demanded that the alumni and staff sign a 'loyalty statement' to the effect that they would abstain from activities detrimental to the occupational forces. As this demand was not met in full, the authorities closed the university.

After the liberation in May 1945, he was blamed for having assumed the rectorate under the Germans and their henchmen and for not having made a firmer stand against them. Though Brouwer's patriotism remained unquestioned, the municipal council of Amsterdam choose to suspend him, and, later, not to reappoint him. Brouwer then experienced the bitterness of the Greek tragedy: in spite of absence of guilt, and having a clear conscience, Brouwer was deeply grieved by fate's injustice (Knegtmans 1998). A. Biemond succeeded him in 1947.

The universal appreciation of Brouwer's scientific work and his colleagues belief in his personal integrity prevailed and he was asked to succeed Ariëns Kappers as Director of Amsterdam's Central Institute for Brain Research. He accepted in 1947, deploying his usual energy in gathering a multitude of enthusiastic research workers around him and shifting the Institute's traditional research focus from comparative neuroanatomy to one of experimental neuropathology. He read various lectures in England and Switzerland, and in Paris he delivered the opening address of the International Neurological Congress (1949).

Six weeks later, during a committee meeting, just before he was to confer the gold medal for cancer research to Prof. N. Waterman at an official ceremony in the Anthonie van Leeuwenhoek Cancer Institute in Amsterdam, Brouwer died a *mors subita*. Dutch neurology lost a giant of a man, in body and in mind.

Note

* Biographical information was obtained from Biemond et al. (1950), Biemond (1961), Droogleever Fortuijn (1949, 1950), Lindeboom (1984), Prick (1949), and Van Valkenburg (1949).

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J.G. Dusser de Barenne *1885-1940* 20

L.A.H. Hogenhuis

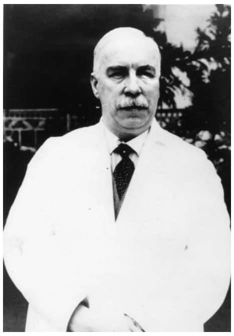

Figure 1. Johannes Gregorius Dusser de Barenne.

Joannes Gregorius Dusser de Barenne was born on June 6, 1885 in the village of Brielle in the Dutch province of Zeeland, the son of Dorothea Vogelzang and Elize M. Dusser de Barenne. His father was the chief of police in Brielle from 1884, and in Amsterdam from 1888. He studied medicine at the University of Amsterdam, graduating in 1908. On October 12, 1911 he married Kate Snellen, daughter of the well-known Dutch ophthalmologist Snellen, who succeeded the great ophthalmic surgeon Frans C. Donders as professor of Ophthalmology at the University of Utrecht. They had three daughters. Mrs. Dusser de Barenne died suddenly in Ithaca, New York, on the May 8, 1931, while accompanying her husband on a lecture trip. Four years later (in June 1935), he married a former student of his at Yale, Emily Lockwood Greene; they had one daughter.

His professional career began in 1909 as teaching assistant in the Physiology laboratory in Amsterdam, where he started his work on the effect of strychnine on the reflex activity of invertebrate ganglia.[1] These initial studies concerned the effect of local application of strychnine on the reflexes of the spinal cord.[2, 3] Seven of the nine papers he published during the period 1909-1911 dealt with the effects of strychnine on various parts of the nervous system. Magendie had already used strychnine (1822) to substantiate his findings concerning the motor function of the dorsal spine roots. In Dusser's hands, the procedure entailed application of small pieces of absorbent paper soaked in a solution of strychnine on to a 1-5 mm area of the exposed spinal cord of the cat or, later, the cerebral cortex of that animal,[5] which rendered the associated cutaneous and deep pressure receptors hypersensitive, thus defining the function of the 'strychninised' area of the cerebral cortex (1916). "Dusser de Barenne quickly grasped the potentialities of the drug as a tool for investigations of the activity of the nervous system, and, in later years he used the alkaloid in connection with many of his most fundamental studies of nervous function" (Fulton and Garol 1940). Further details of these studies are given below. His wide use of this compound as a research tool "won him the nickname he enjoyed - Strychnine" (McCulloch 1940).

He was appointed psychiatrist at the Meerenberg psychiatric institute, north of Amsterdam, in September 1911. He remained there until the outbreak of World War I, engaged in the physiological analysis of decerebrate rigidity[5], earlier described by Sherrington and others, and also of tonic neck and labyrinthine reflexes.[6] Among other things, he established the fact that well-defined action currents can be detected in muscles exhibiting the rigidity of the decerebrate state.

During World War I he served as a medical officer in the Dutch Army in Delft (August 2, 1914 - April 28, 1918). Despite his military duties, he managed to continue research on the tonic contraction of skeletal muscle,[7] publishing fourteen papers in this period, including one on the functional localisation of sensory phenomena in the cerebral cortex[8] and one with J. Boeke on the sympathetic innervation of skeletal muscle.[9]

The fourth phase of his scientific career started in 1918, when he became assistant to Rudolf Magnus at Utrecht. He participated actively in the work of Magnus's team for twelve years, helping to develop the physiological concept of 'Körperstellung' (posture), which earned the Utrecht school international recognition. In addition, between May 1918 and September 1930, he published 38 papers on a variety of subjects including the action of insulin, the metabolism of muscles during decerebrate rigidity, the influence of the vagus nerves on action currents of the diaphragm, and several papers on nystagmus, as well as one with Magnus on righting reflexes in the decerebrate cat and dog.[10] His most important contribution during this period was the result of a few months stay at the laboratory of Sir Charles Sherrington in Oxford in the spring of 1924 where he studied the sensory symptoms produced by local application of strychnine to the cerebral cortex of rhesus monkeys (Fig. 2). The paper describing the results of this investigation[11] became a classic of neurophysiology within five years.

While there, he demonstrated for the first time the major functional subdivisions of the sensory cortex, viz. the areas for the leg, arm and face. This paper was the first of an important series on functional localisation in the cerebral cortex. During 1926, in collaboration with Sager – a scientist who had come over from Bucharest – he used the same approach in experiments on the cat to explore the last relay station of sensation, the thalamus opticus. Thus, by 1927, he had delineated the entire central system subserving bodily sensation with the aid of the technique of local strychninization that he had developed. He had thus clearly and largely anticipated the famous explorations at McGill University and later at the Montreal Neurological Institute by Wilder Graves Penfield (1891-1976), who identified the cortical areas, mild stimulation of which elicited motor or sensory

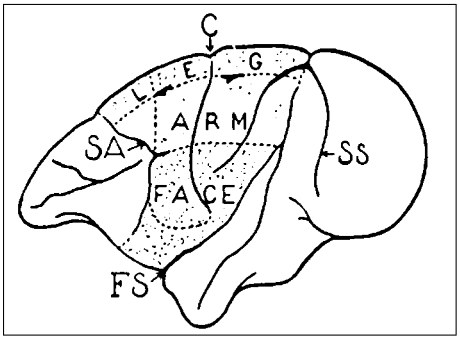

Figure 2.
Map of somatosensory cortex in macaque as outlined by method of strychnine stimulation. Abbreviations used are: C., central fissure; FS., sylvian fissure; SA., arcuate sulcus; and SS., simian sulcus (external parieto-occipital sulcus). (After Dusser de Barenne, Proc. Roy. Soc. 96B (1924), 272-291).

responses, changes in speech and vocalisation, memory of past experience, and visual and auditory effects. Penfield did not start these experiments until 1928, after having returned from Breslau where he had seen for the first time the human electrocorticograms taken from conscious patients in Otfrid Foerster's clinic.

The year 1927 became a turning point in Dusser de Barenne's career. By this time he had, according to Fulton and Garol, "become the foremost of the younger generation of Dutch physiologists." In this year, the physiologists Rudolf Magnus in Utrecht and Nobel Prize winner Willem Einthoven in Leiden both died and a third professor of Physiology, Hendrik Zwaardemaker, retired. The three most important chairs of Physiology and Pharmacology in the Netherlands thus became vacant almost simultaneously. Although second on the list in Leiden, the chairs were for extraneous reasons again occupied by others. "And so it came to pass that the Netherlands allowed the United States to claim one of the most distinguished physiologists the continent of Europe has ever produced" (McCulloch 1940). After some initial hesitation, Dusser de Barenne was persuaded to come to the Yale School of Medicine at New Haven to establish a neurophysiology research laboratory there.

He arrived in Yale with his family on September 24, 1930. His first research collaborator was Clyde Marshall,[12] neuroanatomist, well acquainted with the work of Magnus and Rademaker, with whom Dusser described a release phenomenon induced by isolating a locus of the motor cortex from adjacent cortical areas. The second was Stephen Brody, with whom he studied the effects of hyperventilation on the excitability of the cerebral cortex.[13] These two papers inaugurated a whole series of key-studies on the functional organisation of the cerebral hemispheres in primates. A fruitful collaboration was begun in 1934 with Warren S. McCulloch, [14, 15] who was his devoted and congenial colleague in research for six years. With the subsequent arrival of Leslie Nims[16] and others a team was built that demonstrated the reciprocal relationships between the activity of the cortex and its hydrogen-ion concentration. The research programme inaugurated by Dusser de Barenne at Yale thus proceeded in the most logical manner from the study of the release phenomenon with Marshall via the investigation of the effects of hyperventilation on cortical excitability with Brody, the development of thermocoagulation (a new technique for selective laminar destruction of the cerebral cortex which proved to be a powerful tool for mapping the function of this organ) with Zimmerman, and the study of excitability cycles with McCulloch, to its culmination in 1938-1939[17] when Dusser de Barenne worked with Nims and McCulloch to show how the above-mentioned phenomena were correlated with changes in the hydrogen-ion concentration of the cerebral neuropil.

In his physiological work Dusser de Barenne developed many new techniques such as the strychnine method for localisation of sensory function, laminar thermocoagulation for analysis of the cortical layers, and adaptation of electrical techniques for study of the interaction between specific cortical areas. J.F. Fulton and H.W. Garol, two friends and colleagues, in an obituary in the pages of the *Journal of Neurophysiology*, of which Dusser de Barenne was co-founder and co-editor, stated:

> "He will be remembered for his unyielding faith in the experimental method and for his utter intolerance of those who placed the armchair ahead of the experimental table for solving the problems of physiology. He was a man of strong personality and strong loyalties, and he had a number of heroes. Among those was Claude Bernard, whose portrait was always before him on his desk; another was Carl Ludwig; and the third was his chief at Utrecht, Rudolph Magnus. These were men of action, men of experiment, men who never allowed their deduction to exceed their evidence [...] Although he did not have a formal obligation to teach he offered each year one or two electives, either on the sense organs, or on special phases of the physiology of the central nervous system. Almost invariably he illustrated the lectures by experimental demonstrations into which he had put much time and thought, and usually he ended these amusing and informative discussions in a fever heat of perspiration. The students responded with great warmth of appreciations, for these were lectures unique in their medical experience."

W.S. McCulloch also cast light on these lectures in the obituary he wrote for the *Yale Journal of Biology and Medicine*:

> ."... these lectures combined a continental dignity with amusing turns in phrase and turns of the dynamic lecturer, which were a source of unending delight to the class. No one can, for example, forget his demonstration of nystagmus in the cat, during which he pirouetted around with a cat in his arms, and would stagger back to the blackboard, saying his semicircular canals were more affected than those of the cat. It was great teaching, great devotion to an ideal - the creed of experimental physiology which the students at Yale will not soon forget... "

Any league table of the centres of excellence for experimental physiology in the years 1930-1940 worldwide would have placed Dusser de Barenne's neurophysiology laboratory at the Yale School of Medicine high in the top ten. Known as the 'father of chemical neuronography', Dusser de Barenne showed in subsequent experiments that the electrical disturbance produced by the simultaneous firing of the underlying cells, could be recorded at the nerve fibre endings. This method provided a physiological cross-check of the connections found by the anatomists on dissection of dead brains, but divulged nothing about the pathways traversed from origin to destination; its major benefit was in demonstrating the multiplicity of corticocortical links. Dusser de Barenne demonstrated the wide-ranging extent of such links in the frontal cortex by application of strychnine on either side of the central (rolandic) sulcus, thus greatly intensifying the sensitivity of the organism to somatic sensory stimulation. This was shown first in the cat (1916) and later in the monkey (1924). As soon as the sensory cortex subdivisions were mapped in the monkey he turned to the chimpanzee to discover the finer differentiations of this structure and to obtain a better indication of what might be expected in man. Experiments on the chimpanzee were well under way when Dusser de Barenne died on June 9, 1940. Several unpublished and almost completed manuscripts, and others, for which his notes and conclusions exist, are preserved in the Dusser de Barenne archives at the Yale Medical Library. Chemical neuronography led to the discovery of hitherto unsuspected fibre connections and projections (chiefly nonmyelinated). Some neurophysiologists fostered doubts about the method. The absence of clear-cut findings in some cases could cause confusion about the interpretation of the experimental results. Others, such as Adrian and Moruzzi in England in 1939, elaborated the technique and examined the strychnine-evoked potential with the aid of loudspeaker effects (dramatically described by Moruzzi[18] many years later). After a number of preliminary investigations of the electrical activity of the cortex in 1935-1937, "he [D de B] finally gave permission to put on strychnine" – as McCulloch recalls – "and watch the oscillograph. His face when he saw the first record is as unforgettable as the strychnine spike itself...."

The method of laminar thermocoagulation[19, 20] came to him in a dream, as he recalled later during a conversation with his friends Fulton and McCulloch. The sudden death of his wife in 1931 had depressed him to such an extent that he thought of quitting science. He lay awake night after night, worrying about the impasse in his laboratory work for lack of a method to determine which layers of a cortex were requisite for sensation. Finally, in the middle of one long lonely night he thought of getting up and having breakfast, but dozed off. In his dream, he saw an egg cooking slowly. He jumped from his bed, rushed to the laboratory, heated a brass rod in boiling water, and applied it to the cortex of an experimental animal. Within twenty minutes, the method of laminar thermocoagulation was at his fingertips (McCulloch). "It was equally characteristic of the man that he used that insomnia which never left him as an opportunity to become most erudite," McCulloch goes on to say.

During the 1930s, voluminous evidence accumulated for what came to be termed the 'feedback' of information between cortex and thalami. In a presentation on this topic to the Boston Society of Psychiatry and Neurology, B. Brouwer (1933)[21] from Amsterdam embellished his talk with slides, drawings and glass models, then much in vogue, depicting centrifugal and centripetal brain systems. He acknowledged the key role that Dusser de Barenne's neuronographic techniques had played in his researches, and reported: "A very remarkable fact is this, that many fibers descending from various parts of the cerebral cortex, go back to all their [thalamic] nuclei."

Dusser de Barenne argued that the bilateral 'thalamic syndrome' of acute cutaneous hypersensitivity after application of strychnine to a small area of the sensory cortex, despite the novocain decortication of the surrounding areas, must be due to "setting on fire the cortex of the whole sensory arm area and... those [representational] portions of the optic thalamus"[22] (p. 284). This was Dusser de Barenne's contribution to an elucidation of a syndrome that had long baffled clinicians. In his assumption of a close functional relationship between cortex and thalamus (Fig. 3), Dusser de Barenne joined the company of those clinical investigators, among them Head and Holmes, von Monakow and Dejerine, who entertained the idea of an interactive information flow between cortex and thalamus.[23]

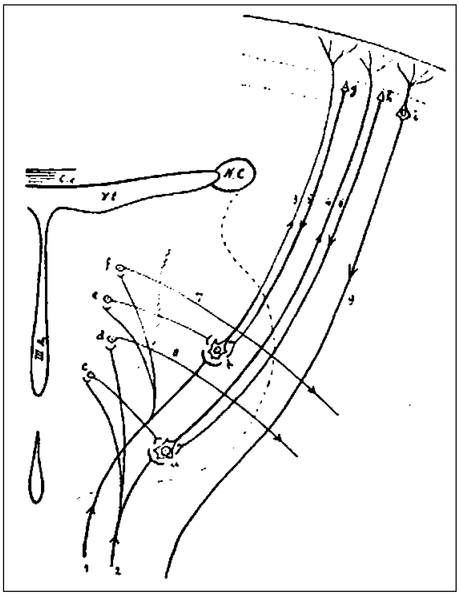

Figure. 3.
The scheme of reciprocal action between cerebral cortex and thalamus, as sketched by the 'father of neuronography'.
a, b - ventrolateral thalamic nuclei; c, d, e, f - medial thalamic nuclei; g, h - corticothalamic neurons; 1, 2 - afferents from the periphery; 3, 4 - corticopetal fibers to sensory cortex; 5, 6 - corticothalamic fibers; 7, 8 - extrapyramidal fibers; i, 9 - corticifugal, pyramidal fibers. (From Dusser de Barenne (1935) 285, Fig. 79, x1.)[22]

At that time, the ground was ready for an entirely new approach to the understanding of neural networks. The benefits derived from the method permitting demonstration of the wide-ranging corticocortical, corticothalamic and other connections developed at Dusser de Barenne's laboratory elicited great public interest. A front-page article in the New York Times of 31 December 1936 brought readers the news on this topic under the headline '"Inside telephones" in Brain': "Dusser de Barenne, interviewed, claimed the new 'brain circuit' might be likened to an 'interoffice' communicating system which linked the cerebral cortex with the thalamus. Thus he said a mutual exchange of messages goes on constantly between the old (the seat of emotions) and the new brain (seat of intellect) on the one hand, and the sense organs and the muscles on the other hand...."

By 1938, the concepts of thalamic cytoarchitecture and cortico-thalamic connections were fairly well established, the former in part through the work of Cajal and the latter equally so through neuronography as elaborated by Dusser de Barenne and McCulloch.[24] The occipital cortex occupies a position of prominence in the history of the human brain – anatomically, physiologically and behaviourally – because it is the primary cortical projection of the most extensively studied of the senses.[23] In 1934, he stated that vision "is, I think, the function which in the higher mammals has become most corticalized" (Dusser de Barenne 1934, p. 103[25]). Dusser based his opinion on the fact that vision has a distinct and stable localisation, in contrast to other functions, which are more diffuse and may show marked repair of lost function. "His statement was made prior to discovery of many additional cortical centres concerned with vision whose relation to the phylogenetic response to evolutionary influence is still not understood."[23]

Hughling Jackson (1862-1907), the conceptualist, a man of few words and often with second thoughts of what he had published but with emphasis on the non-existence of sharp boundaries around cerebral functional areas, would have nodded his assent hearing Dusser's views on 'corticalisation'. He would have been comfortable with Dusser's warning (1934) "about the parochialism of designating" localisation "for a function that so patently takes place in many parts and levels of the brain."[23] Dusser preferred 'corticalisation' as the more accurate term.[22, 24-26]

The close collaboration with Warren S. McCulloch (1898-1968) has been mentioned several times above. Further details of McCulloch's life are given by Marshall and Magoun (1998). From an early interest in philosophy, McCulloch trained as a psychiatrist; his attainments eventually gained him memberships in an unusually broad array of professional societies, representing the fields of neurology, anatomy, physiology, mathematics, biological psychiatry, arts and sciences. Such diversity was lodged in a man who was dubbed a "rebel genius" (Gerard 1970) and whose intense eyes, unfashionable beard and abrupt manner did not inspire general confidence. Nonetheless, he was a magnet to those neuroscientists who could conceptualise beyond impulse conduction and the neuromuscular junction. The collaboration between Dusser de Barenne and McCulloch bore the richest fruits during the last six years of the former's life, due to the synergy of their different mind-sets and their unusual friendship. It would thus seem appropriate to conclude this portrait by citing McCulloch (1940) once more: "To succeed at all any man so heartily kind and trusting must carry a shield. To the outsider he appeared suspicious and as blunt as only those can afford to be who are completely humble to the fact. But once past that guard all were compelled, by his very openness, to give him their best."

Fulton, another friend, wrote later from New Haven: "The sudden death of Professor Dusser de Barenne on June 9, 1940, occurred at a time when international communications were seriously disrupted, and many of his colleagues in Europe were therefore long unaware that his brilliant career had been brought to a premature close when he was but fifty-five years of age and at the height of his powers..."

Acknowledgements

The help of the Yale Medical Historical Library, Mrs. Tony A. Appel and Mona Florea is gratefully acknowledged.

Extensive use has been made of the obituaries written by Dusser de Barenne's close friends and colleagues J. F. Fulton and H. W. Garol (Fulton and Garol 1940) and W. S. McCulloch (1940) in the preparation of this biographical note.

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F. Grewel *1898-1973* 21

J.A.M. Frederiks

Frits Grewel was born on November 19, 1898 in Amsterdam, where he also grew up. His father was a diamond cutter of repute. His mother, a Jewess, was widely read and educated.

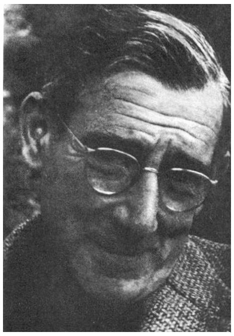

Figure 1.
F. Grewel.

The socialist convictions of his parents influenced him deeply and lastingly. Later on in life, in the late 1960s, he would sympathise with the protest movements among students. Initially, he dreamt of an artistic career, but he could not detect the specifically required abilities in himself. His poor health and periods of serious illness often forced him to take it easy, which provided him with opportunities to read widely beyond his medical education. In this way he studied anthropology, sociology and criminology during his student years at the medical school in Amsterdam. He qualified as a physician in 1925, subsequently specialising in neurology and psychiatry in the Wilhelmina Gasthuis of Amsterdam (head at the time was Prof. Dr K.H. Bouman). The subject of his M.D. thesis (Amsterdam, 1935) dealt with the development of denture (his promotor was the anatomist Prof. Dr M.W. Woerdeman).

He was appointed head of the psychiatric outpatients department of the Wilhelmina Gasthuis in 1930. Soon after he opened a special psychiatric (and neuropsychological) outpatients department for children, the first one in the Netherlands. For a short period he headed the psychological laboratory of the psychiatry department at the Wilhelmina Gasthuis.Grewel was one of the first psychiatrists in the Netherlands to cooperate with a clinical psychologist in the clinic. Later, he would advocate the establishment of some more multi-disciplinary teams.

The German occupation forced him to discontinue his private practice. In that period, he made a study of the sociology of Amsterdam Jewry and undertook a systematic follow-up study over eight years of a case of Pick's disease (which, owing to post-war conditions, was not published until 1955).

Grewel was given a lectorate in child psychiatry at the University of Amsterdam in 1954, and, in 1965, he was appointed professor of orthopedagogics with the Faculty of Social Sciences at the University of Amsterdam, as well as Head of the Institute of Orthopedagogy in Amsterdam. He retired in 1969. Grewel died following a short illness of the stomach on October 9, 1973.

In his time, Grewel was one of the very few neurologists alive (others being, for example, Eberhard Bay, Macdonald Critchley, Anton Leischner and F. Panse) who drew attention to the importance of linguistics in aphasia. He participated in many of the international symposia of linguists and neuropsychologists (e.g. The International Association of Logopedics and Phoniatrics, The Annual Symposium of the Aphasiologists, The International Congress on Orthopedagogics, The International Neuropsychological Symposium). He was among those who organised the first meeting of the International Neuropsychological Symposium (in the beginning called 'Neuropsychopathological Conferences') held in Mondsee, Austria, September 1951; he was one of the founding members of the Board of Associate Editors of the new journal *Neuropsychologia* (Oxford 1963); he lectured at the National Hospital in London (1951); and it was Grewel who stimulated Welman and Frederiks to found a Netherlands Society of Neuropsychology (1970) (see also chapter 15).

Grewel was an exquisitely erudite man with a fabulous memory, and with expertise beyond his proper specialities, evidenced by his knowledge of antiques and a variety of artistic expression forms. He possessed a valuable library (fig. 2). Grewel was a close friend of the well-known Dutch painter of 'mystic realism' Carel Willink (1900-1983). Grewel's dedication to his patients, both in private practice and in the clinical setting, made them adore him, particularly the children and their parents. He is remembered for his humanity and charm, and a good many know him as a raconteur and a baritone singer of folk songs in several languages. He was a careless dresser and inclined to neglect the administration of his records and his fees, which were already absurdly low.

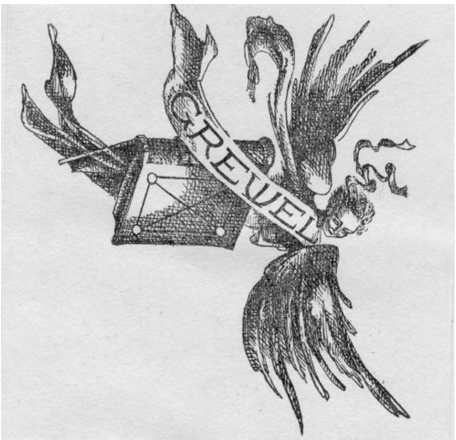

Figure 2.

To his colleagues he was known as a somewhat impatient, critical, but open and pleasant personality. In discussions his expertness and originality were striking. He was known for his criticism of any dilettantism. As a born teacher, he always emphasised the need of painstaking clinical evaluation of every individual child in his care. Grewel was "an exceptional man of great wisdom and yet simplicity" (Critchley 1990). From his own personal experience the present author agrees with this statement.

A good deal of his numerous scientific publications were in Dutch; other, of course more well-known, papers were in English, German or French. He wrote on every field of his specialities: (child-) neurology, (child-) neuropsychology, (child-) psychiatry and orthopedagogy. Disorders of speech and language were his special interest, such as aphasia, and especially linguistic disturbances in aphasia. We mention here only the studies on asemiotic disorders, dysarthria, acalculia, stammering, cluttering, developmental dyslexia, infantile autism, multi-handicapped deaf children, and cerebral palsy. Neurological studies included the Kleine-Levin syndrome, parietal lobe symptomatology, the punchdrunk syndrome in boxers, manganese poisoning (with E. Sassen), congenital suprabulbar paralysis, and trichlorethylene intoxication.

To conclude we present a few sketches of Grewels ideas:

Grewel repeatedly stressed the importance of a systematic neurological examination of children with disorders of language development and/or learning disabilities. "Much of what seems psychological in reality is neurological." One may find slight abnormalities in the pyramidal or extrapyramidal system, pathological reflexes, disorders of motor function, delayed establishment of manual preference. These minor neurological aspects often remain unknown and unobserved by inexperienced clinicians.

According to Grewel, normal language is made up of a polydimensional system of signs, comprising:

1 a system of distinctive sound-elements, or phonemes;
2 a system of words, or phonetic-semantic units;
3 a system of diversity in word-formation;
4 a system of diversity in sentence-formation;
5 a system of accents (pitch, length, stress).

In *Aphasia and Linguistics* (1951), Grewel distinguishes the following linguistic disorders in aphasia: 1. lexical losses; 2. phonemic disturbances; 3. paraphonemia; 4. paraphasia; 5. agrammatism and paragrammatism; 6. disorders in the system of accents; 7. disturbance in non-verbal forms of communication.

In his study *Classification of dysarthrias* (1957), he classified the different types of dysarthria, following a historical review of the disorder, which began with Kussmaul (1822-1902), who gave the first classification of speech disorders (in: *Die Störungen der Sprache*, 1885). On the basis of neuroanatomic and neurophysiologic principles Grewel listed fourteen types of dysarthria, including cortical, subcortical, peduncular, supranuclear, bulbar, cerebellar, diencephalic, mesencephalic and peripheral. In addition, he discerned 18 forms of stuttering, the pathogenic factors of which are developmental, linguistic, neurotic or neurological. Grewel indicated that stuttering and cluttering might develop especially during the period when speaking does not as yet follow thought (cluttering), or when the child has not acquired sufficient language material to meet the existing impulse to communicate (stuttering). Physiological stuttering and cluttering of this kind are normally overcome, but they develop further when neurotic or neurological causes interfere.

In his papers on acalculia ('the paradigm of semiotic disorders') Grewel distinguished primary and secondary acalculias. He divided primary acalculia into asymbolic acalculia and asyntactic acalculia. Secondary acalculia occurs with aphasia and with the Gerstmann syndrome. In patients with aphasia the interference of expressive difficulties with calculation complicates the disorder. Paraphasic responses may create the impression of acalculia. Grewel emphasised, that "in acalculia it is not a biological function, but a sociogenic, learned behaviour or performance, a conditioned semiotic system, that has suffered."

Grewel is remembered by many neurologists for his outstanding and pioneering work in the fields of neuropsychology, especially the linguistic approach to the study of aphasia, and for his research into the mechanisms of developmental language and speech difficulties in children as well as his numerous studies on learning disabilities. "He left footprints which are still detectable by those who are sensitive and sympathetic" (Critchley 1990). He really was an epoch-making paediatric neuropsychiatrist.

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G. Jelgersma *1859-1942*

22

P. Eling

At the celebration of the 50th anniversary of the Netherlands Society of Psychiatry and Neurology in 1921, Leendert Bouman, chairman of the meeting, introduced the two main speakers of the meeting, Winkler and Jelgersma, thus:

Figure 1. Gerbrandus Jelgersma.

> "May I finally recall a simple fact from the meeting in 1885. In the report of that meeting we read: Jelgersma, prosector at Meerenberg, and Winkler, lecturer in psychiatry in Utrecht, have been accepted as members of the Society. There is no need to elaborate in detail how much both these men have done for the Society. They were both chairman twice, later several times editor of the *'Bladen'**. They were members of numerous committees and put their signature under a series of reports. But apart from these, a large series of contributions, published in the 'Bladen' or elsewhere, testify to their serious scientific work, which increased the fame of Dutch psychiatry and neurology. An elderly statesman once told me with a certain pride that both here and abroad so many statesmen remained so fresh at high age and were still capable of serving at difficult posts. Is not this true also of our two pioneers, who fortunately still have not reached high age, even though they belong to the group that participated in celebrating our silver and golden feast? Moreover, they were, next to Van Andel, our official speakers, and naturally have been elected again to discuss the history of our discipline over the last 50 years" (Bouman 1921, p. 318-319).

Jelgersma and Winkler were clearly regarded as the two most significant members of the Society. Whereas Winkler remained faithful to the biologically oriented neuropsychiatry of the late 19th century, Jelgersma decided, around 1910, to embrace Freud's psychoanalysis. Winkler dominated in Amsterdam and Utrecht, Leiden was Jelgersma's kingdom.

Short biography

Gerbrandus Jelgersma was born November 1, 1859 in Doevere, a little village by the river 'Bergse Maas', approximately ten kilometres north of Waalwijk in the southern province Northern Brabant. He was an atheistic – so it appeared later – member of a

Figure 2.

Frisian Protestant ancestry: his father, grandfather and great-grandfather were all parsons. According to his biographer, former student and successor to the psychiatry chair in Leiden, Eugène Carp (1895-1983), he already behaved a bit curiously as a child (Carp 1942): he did not care for friends and preferred to stroll around in open countryside. He was a mediocre student and went to high school in Alkmaar. He studied medicine in Amsterdam from 1878 until 1885. Psychiatry was not yet part of the medical curriculum and he lacked a decent knowledge of the structure of the central nervous system and its relation to behavioural disorders.

When he became prosector in the mental health institute 'Meerenberg' near Haarlem, he had ample opportunity to make up for this lack. He was also confronted with a wide variety of neurological and psychiatric syndromes. He enjoyed doing postmortem examinations and practiced the techniques necessary for studying nervous tissue under the microscope. In the institute reports one can find numerous reports of his observations, often supplemented with theoretical considerations.

In 1892, the psychiatrist Jacob van Deventer, director at Meerenberg, advised Jelgersma to switch the focus of his work to criminal anthropology. In Europe, the discussion had started on the question whether criminals could be held responsible for their misbehaviour. Of course, this was triggered by the work of Lombroso, who also visited the Netherlands on the occasion of the International Congress on Criminal Anthropology in Amsterdam in 1901. Jelgersma explored the new area and attended the conference on criminal anthropology in Brussels in 1892. He left Meerenberg in 1894 when he was appointed 'privaat docent' in criminal anthropology and forensic psychiatry at the University of Amsterdam. In his oratory lecture he formulated the central question for the new discipline: is there an anatomy of the criminal? He argued that the prison should become a place for scientific research, in particular for anatomical studies. He also became director of a clinic for mental patients in Arnhem. Jelgersma was appointed editor of *Psychiatrische en Neurologische Bladen* in

1897, when the journal of the Netherlands Society of Psychiatry and Neurology was renamed.

He must have felt like a fish in water when he was invited to occupy the newly founded chair of Psychiatry in Leiden in 1899. Originally, the chair had been offered to Winkler, but he declined, arguing that he could not be missed in Amsterdam while Leiden would be able to find another good candidate. According to the local authorities, the chair was meant for demonstrations of clinical patients and scientific research, consisting of neuroanatomical studies. In his oratory lecture, entitled 'Psychology and Pathological Psychology' one can already trace Jelgersma's interest in the psychological mechanisms underlying behavioural problems. And with 'psychology' he meant 'experimental psychology' without referring to specific authors. But from the description it is clear he is referring to the Wundtian tradition. Psychology at that time was recognised as an independent scientific discipline. Wundt had provided it with a decent status by developing an experimental approach to the workings of the mind. Ribot, and after him Janet, applied the new insights to the interpretation of mental disorders of psychiatric patients. In the Netherlands, Heijmans and Wiersma demonstrated the value of psychology, both as a fundamental and applied academic discipline in Groningen. Jelgersma recognised that the phenomena he observed in his patients could contribute to the insights in the workings of the mind. Psychiatry (or rather 'the psychiatrist') should not only develop knowledge of the substrate, but it should also focus on its function, not in a physiological sense, but in behavioural terms. In the concluding paragraphs of his lecture he was quite outspoken: "'Psychiatry is a natural science just as much as psychology is" (p. 32).

Bolland, professor of Hegellian philosophy at the Leiden University from 1896, strongly opposed Jelgersma's view (Otterspeer 1995). He invited him to engage in a public debate, but Jelgersma declined the offer. However, in 1906 Jelgersma felt a strong need to react to Bolland's belligerent lectures, since he was convinced that Bolland's influence on the students' minds was nefarious. Jelgersma was not familiar with philosophy; he regarded metaphysics useless. Jelgersma formulated his criticism in the form of a 'public letter', a pamphlet of 21 pages. This letter elicited many negative reactions, particularly in Leiden, but also in other areas of the country, as well as from individuals who could not be regarded as Bolland's friends. Jelgersma was accused of being too disrespectful towards his colleague. Three of Bolland's former students defended their teacher and each published a pamphlet, arguing that Bolland could not be regarded a founder of a sect with such critical followers (Grondijs 1906, Fraenkel 1906, van den Bergh 1906, Otterspeer 1995). Jelgersma, convinced of his good intentions and the correctness of his scientific approach, did not find it difficult to defend himself against the criticism, which was also ideologically coloured. He knew very well what he was talking about. Moreover, he was not interested in general recognition.

The national and local government cooperated closely to establish proper conditions for the care of psychiatric patients. A psychiatric institute called 'Endegeest', located in the village Oegstgeest, near Leiden, was founded. On Jelgersma's appointment in 1899, it was agreed that a new sanatorium should be built for patients with 'nervous diseases'. 'Rhijngeest', situated next to Endegeest was opened in 1903. It was constructed according to Jelgersma's wishes and it was meant to serve as a matrix for Jelgersma's teaching of psychiatry, accordingly containing a neuropathological and a psychological laboratory. Following Jelgersma's advice, it was decided to build a unit for juvenile patients. This institute was opened under the name 'Voorgeest' in 1912. Although it was a separate unit, organisationally it was related to Endegeest and Rijngeest. A.H. Oort, who was Jelgersma's first graduate student, acted as medical director of the institute from 1905 until 1934. G. Janssens assisted Jelgersma in his neuroanatomical work, experimental psychological studies and later also electrical work.

In 1907 Jelgersma acted as chairman of the First International Conference for Psychiatry, Neurology, Psychology and Care for Lunatics, held from 2 until 7 September in Amsterdam (Stroeken 1997). Many famous neurologists and psychiatrists attended the meeting, for instance, Pick, Vogt, Oppenheim, Westphal, Monakow, James, Weir Mitchell, Marie, Babinski, Lombroso, Marinesco and Bechterew. Governments of 23 countries had sent representatives. Hystery was one of the central themes and the 'Freudian method' was heavily discussed. Although the atmosphere was essentially anti-Freud, every psychiatrist in the Netherlands was familiar with his ideas. At this conference, Jelgersma demonstrated the first series of brain preparations he had worked on assiduously in 1906, and which would finally be published in his magnificent atlas in 1931 (see below). He also read a paper on civilisation as a predisposing factor for the development of mental disorders.

According to Carp, one can make a distinction in Jelgersma's work between the period before and after 1914. In that year, Jelgersma was elected 'Rector Magnificus' of Leiden University. In his rectoral address, 'Unknown mental life', he argued that psychology should not only address conscious processes but also (childhood) memories that lay dormant, unconscious. The dream is a phenomenon at the edge between conscious and unconscious mental phenomena. He discussed dreaming in healthy individuals but formulated the hypothesis that if a dream reflects the emotional condition of an individual, then it is obviously of central significance for the study of patients with nervous diseases. Freud was astonished and enthusiastic that an official psychiatrist spoke in favour of psychoanalysis in a public lecture (Stroeken 1995). Jelgersma thus played an important role in the reception of psychoanalysis in the Netherlands. And yet, he was not a psychoanalyst *pur sang*. To him, psychoanalysis could be regarded as part of psychopathology, unable to replace the whole of traditional psychiatry. Moreover, he welcomed the Freudian explanations for seemingly incomprehensibly associated phenomena that could be derived from it, but he did not believe in the treatment procedures (Rooijmans 1998). His personal view on this matter may have triggered the founding of a second group of analysts, shortly after the Dutch Society of Psychoanalysis had been established in 1917. In 1920, the Leiden Society for Psychopathology and Psychoanalysis was created, consisting mainly of Jelgersma and his students.

Jelgersma taught general psychiatry and neurology, as well as clinical psychiatry, forensic psychiatry and neuroanatomy until 1919. It is difficult to obtain a good impression of what kind of teacher he was. His lectures were well attended; in fact, it is reported that the students objected about a lack of space and fresh air. The popularity of the lectures was certainly also due to the demonstrations of patients (Rooijmans 1998). In 1913, he left the teaching of neurology to some extent to his co-worker Ernst de Vries (1883-1976), who became completely responsible for this task in 1919. After de Vries left for China in 1925, he was succeeded by Abraham Gans (1885-1971), who was appointed as lecturer in neurology. The separation of the two disciplines had begun. Around 1920, Jelgersma made a sharp distinction: psychiatry was not an ordinary medical subject, it required not only 'explanation' but also 'understanding' or insight. It was both a natural and mental science. A psychiatrist had to be both a physician and a psychologist.

In addition to his lectures in the medical curriculum, which were apparently rather well received, Jelgersma supervised 15 theses. Three concerned neuroanatomical topics, five dealt with a psychoanalytic issue and three may be regarded as experimental psychological studies (Rooijmans 1998).

Jelgersma retired with a valedictory address on 28 October 1930 to a large audience of former students. In this lecture, he discussed the 'wake-up dream', a dream in which the content is connected to an external stimulus that awakens the sleeper. In contrast to his firm statement when he assumed office, namely that psychology is a natural science and experimental in nature, Jelgersma's psychology now appeared to be of a speculative nature, not dissimilar to that of many other continental psychologists. He continued his neuroanatomical studies and finished his most important project, the neuroanatomical atlas, in 1931, as well as the monograph on the brain of water-mammals in 1934.

He died on August 17, 1942 in Oegstgeest. According to Rooijmans (1998), Jelgersma became the most influential psychiatrist of his generation. At the same time, he was also regarded as one of the best neuroanatomists in the country and, because of his neuro-anatomical and neuropathological studies, was regarded, together with Winkler, as the founding father of neurology in the Netherlands.

Publications

The majority of Jelgersma's papers (usually some three per year, with the exception of 1888 when he published six articles) appeared in the *Psychiatrische Bladen* (later, *Psychiatrische en Neurologische Bladen*) and the *Nederlands Tijdschrift voor Geneeskunde*. Occasionally, he wrote in German or French journals. In 1886, he published his first article, a paper on a patient with aphasia, soon followed by a paper on a topic that would keep his interest for the rest of his life: cerebro-cerebellar coordination, the role of the cerebellum and its integration with the functions of the cerebral hemispheres.

He published a psychiatric handbook *Leerboek der functionele neurosen* (Textbook of functional neuroses) in 1897. Here, one finds extensive discussions of neurasthenia and hysteria. He endorsed the views of Pierre Janet on hysteria and opted for a psychological interpretation. His notion of 'functional' disorders differed from that of many of his colleagues, who believed that ultimately, it would be possible to point out the organic disorder causing the disease. Jelgersma used the notion of 'short circuiting' to describe the temporary disfunctioning, indicating that the nervous tissue itself remained intact.

His move from the Meerenberg institute to a private neuropsychiatric practice in Arnhem did not interfere with a steady stream of publications on neuroanatomy and neuroanatomical techniques, neurological and psychiatric disorders, forensic psychiatry and the care for psychiatric patients.

Jelgersma summarised his findings on paralysis agitans and chronic chorea in a short note in the *Neurologische Centralblatt* in 1908. He claimed that in paralysis agitans the three generally recognised neuropathological findings (perivascular gliosis, strong pigment degeneration in the cells in the anterior horn of the spinal cord, and the general atrophy of the nervous system) are accidental symptoms. He described atrophy in several areas, such as the lenticular ansa, the thalamic nuclei and the radiations of the substantia reticularis. He argued that mainly cerebellar pathways were affected. In cases of Huntington's chorea he found the head of the caudate nucleus to be reduced by a third, which was the first documented essential change in this disease.

In 1911 a new textbook appeared: *Leerboek der Psychiatrie* [Handbook of Psychiatry]. It consisted of three volumes, together more than 1200 pages. In the introduction, Jelgersma illustrated his 'credo', which was the same as Griesinger's and mainstream German neuropsychiatry: psychiatry is the theory of brain disorders. He distinguished between objective (organic) and subjective (mental) phenomena. The methods of clinical psychiatry should be purely natural-scientific. Both objective and subjective phenomena of the pathological symptoms should be studied using experimental methods. The relation between objective and subjective phenomena was not clear: he believed that all the mental processes are related to nervous processes.

In this book, Jelgersma introduced an original classification of psychoses in two groups: endogenous psychoses ('kiem-psychosen') and intoxication psychoses. The first (with manic depression as the core syndrome) develop on the basis of a deviation of the underlying structure, are largely inherited, and mental processes are not essentially disturbed but deviate in intensity; the latter result from intake of abnormal substances, inheritance can play a role, and symptoms look weird. Only intoxication psychoses may lead to dementia. According to Carp (1942), Jelgersma's vision resembled that of Emil Kraepelin, as laid out in his *Lehrbuch der Psychiatrie*. Even though Jelgersma pleaded for a significant role of psychology in psychiatry, he remained convinced, nevertheless, of the natural scientific approach and believed in an empirical basis. In the 2nd edition of his '*Leerboek*', which appeared in 1917, he did not modify his views. It was not until the 3rd edition, which was published in 1926, that he changed the text in many places, revealing his shift towards psychoanalysis.

A central topic in Jelgersma's research was the function of the cerebellum. His interest was aroused already at Meerenberg. He was familiar with the work of Marchi and Luciani, and based on their insights and his own neuropathological and comparative anatomical studies, Jelgersma developed an original view on the coordinating role of the cerebellum. He noted an evolutionary relation between pathways, connecting bi-directionally the cerebellum and the cerebral hemispheres on the one hand, and the appearance of intellectual functions on the other hand. He referred to these pathways as the 'intellectual pathways' in a paper in 1890. Stimulated by the work of Ramon y Cajal, he investigated the optical system of the pigeon and argued in 1895 that Cajal's finding of centrifugal (motoric) fibres in the posterior root refers to the same principle as his intellectual pathways and suggested this 'arc conduction' ('boog-geleiding') principle holds for the entire nervous system. Having also had the opportunity to examine patients with cerebellar disorders, such as cerebellar anarthria and Friedreich's disease, he maintained that the cerebellum is also important for the coordination of speech movements; however, only bilateral lesions would result in cerebellar anarthria. He presented his views on the role of the cerebellum in a monograph *De physiologische betekenis van het cerebellum* [The physiological function of the cerebellum] in 1904. A new version of his views appeared in a paper in 1915 *(The function of the cerebellum)*. Taking into account anatomical studies on the nerves of the muscle sense and equilibrium, he argued that the cerebellum plays a role in coordinating movements at an unconscious level. It is a reflex-like error correcting system, whereas the cerebrum is responsible for conscious adaptations. The cerebellar system is active in posture movements (balance, walking), skilled movements and expressive movements (speech and mimics). Essentially it means, Jelgersma argued, that the function of the cerebellum is the coordination of voluntary movements. He revised and enlarged his 1915 paper and summarised his findings in a new monograph *De kleine hersenen, anatomisch, physiliogisch, and pathologisch beschouwd* [The cerebellum, anatomically, physiologically and pathologically considered], which was published in 1920.

Jelgersma wrote an interesting paper, called *Over Schakelingen* [On Connections] in 1928. One may regard it as a precursor of Hebb's views on the neurophysiological basis of learning. The notion refers to new temporary connections that are made in any function or in any nervous process. They contrast with preformed connections. They allow for learning and variation in development. Thus, the nervous system is able to produce very complex functions. In essence, Jelgersma argues that no specialised (dedicated) systems or functions need to be inborn; they can develop because of the principle of connectivity, or to put it differently, Jelgersma described the idea of a self-generating neural network.

His atlas *Anatomicum Cerebri Humani* appeared in 1931. Jelgersma had collected all the material for it in 1906, together with his assistants Miss Ketjen and the physician Wolfensperger. Jelgersma claimed that the slices were still in excellent condition. He regarded his atlas superior to the one by W. Spielmeier (1924). The atlas contained 168 photographs of slices in three different planes (longitudinal, transverse-coronal and horizontal). Due to a lack of time, it had been impossible to write texts describing these plates. A major part of the original slices can still be seen in the neuroanatomical museum in Leiden, thanks to the restoration efforts of Prof. A. Luyendijk-Elshout.

In 1934 he published *Das Gehirn der Wassersäugetiere. Eine anatomische Untersuchung* [The Brain of Water Mammals], which studied in particular the dolphin, sea cow, seal, and the common otter. The study focused on the question to what extent altered external conditions determine the remarkable features of the nervous system in these water mammals. His final paper, dealing with the pathways to the hippocampus, was published in 1939, when he was 80 years old.

Personality

It is of course impossible to present an objective picture of the person Gerbrandus Jelgersma. Carp was clearly aware of his limitations, having been his student and a close co-worker for some twenty years. Yet, some of the features described by Carp seem to be compatible with the data that are available in the form of his publications and his appearances at conferences.

He was, first of all, an excellent researcher. He studied the brain without interruption for approximately 35 years. Many contemporary neurologists were mostly interested in the motor system, the underlying mechanisms of overt behaviour. Jelgersma, however, emphasised psychopathological phenomena, assuming that they would provide a window to the relation between brain and mind. Perhaps this can be related to what Carp called the tendency to look for a synthesis. Carp described this as a general feature; it is clearly visible in his scientific work. At a general level he integrated different disciplines. A central topic of research was the coordinative function of the cerebellum.

Jelgersma can be described as a ‘workaholic’ and he preferred to work on his own, a typical lone wolf. He was reluctant to attend to domestic affairs. He was not married and was also not interested in social and cultural life, and even had little contact with his fellow professors. In a sense he was ambitious: he wanted to understand what he saw under the microscope, and he wanted to present his results to his colleagues, but did not invest much energy in convincing others of his opinions. It was not so much status as sheer curiosity that seems to have been his major drive. He hated authority and accordingly opposed religious views that claimed ‘the’ truth; for the same reason he disliked philosophical system builders. Jelgersma was not a religious man. People often accused him of materialism, which is not really surprising, if one reads his papers. He himself claimed that he adhered to psychophysical parallelism. His interest in the many aspects of his work kept him busy and consequently he was not very interested in organisational matters such as the construction of new clinics. He had clear preferences, but if his wishes were rejected, he did not insist.

In certain respects, he was an unorthodox man. In his outlook and in his contact with patients and students, he lacked the formal approach, to which his fellow professors adhered so much. In his work, he was not afraid to integrate the results and views of colleagues and yet, he remained faithful to the 'traditional' neurobiological approach and empirical research as the basis. He was rather insensitive to what others thought about his work. Jelgersma was indeed of international stature. Nevertheless, his influence in the international literature was not large.

Note

* 'Bladen' refers to 'Psychiatrische en Neurologische Bladen', the journal of the Netherlands Society of Psychiatry and Neurology.

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H.G.J.M. Kuypers *1925-1989* 23

L.C.M. Moll

When Hans Kuypers died in Cambridge,U.K., at the age of 64 he was an internationally renowned neuroscientist, who left an impressive list of 126 papers, many of which are frequently cited, the last of which was published posthumously in 1990.

Figure 1.
H.G.J.M. Kuypers.

Biography and scientific contributions

Born on September 9, 1925, in Rotterdam, as the only child of upper middle class parents, he passed through high school ('Gymnasium') there, with interruptions due to wartime circumstances. After his final examination in 1945, he began studying medicine at Leiden the same year. During his medical studies he worked from 1947 tot 1950 as a student assistant in neuroanatomy and histology under prof. S.T. Bok, who would later be the supervisor for his doctorate thesis. It was here that Hans Kuypers became impressed by the teaching of the neuranatomist Walle Nauta (1916-1994), so much so that during his subsequent summer holidays he visited Nauta twice in Zürich to learn the optimal staining methods for identifying degenerating axons. Later in Zürich Nauta developed the silver impregnation technique, which still bears his name as the Nauta method, by which degenerating axons and normal fibres could be more clearly distinguished from each other than by the older methods (Lemon 1990).

Meanwhile Hans Kuypers finished his doctoral work in Leiden, and in 1952 he defended his doctoral Ph.D. thesis *Fibre connections of the midbrain central grey* (supervisor Prof. S.T. Bok, advisor W.J.H. Nauta). After two years of internships in various hospitals he graduated as a Medical Doctor (MD) in 1954. In that same year he married Maria (Toetie) Schaap, a technician in the hospital lab. The marriage was blessed with six children, two sons and four daughters.

Wishing to become a neurosurgeon, he moved to Groningen to take up a residency in the neurological department of Prof. J. Droogleever Fortuyn, a clinical neurologist with a strong affinity to neurophysiology and neuroanatomy. "The clinical work however did not stimulate his mind" (Phillips and Guillery 1992), and a year later, in 1955, he accepted a position of Assistant Professor of Anatomy at the University of Maryland, Baltimore, probably helped by the influence of Nauta, who by this time worked in nearby Washington DC.

THE TIME IN MARYLAND AND CLEVELAND USA

In Maryland, Hans Kuypers started a most fertile line of research into the anatomy of movement, linking morphology to function. In studies of cortical connections to the brainstem, he found, among other things, that the motor cortex also receives ascending fibres, e.g., from sensory nuclei in the brainstem and in the spinal cord. Moreover, the post-central sensory cortex not only receives fibres from, but also sends fibres to sensory nuclei as well as to the ventral horn of the spinal cord, both serving as feedback systems (Kuypers 1960). It was Hans Kuypers who unequivocally showed that the pyramidal tract originates not only from the primary motor cortex but from many cortical areas, and that it also conveys 'sensory' fibres (Richard Passingham, Oxford, UK, personal communication). After these studies he gradually came to realise that the motor capacities of the various descending fibre systems are determined not by their areas of origin but rather by their termination areas in the brainstem and the spinal cord, i.e., by the interneurons and the motoneurons upon which these descending fibre systems converge. Therefore, studies of the organisation of the motor system were begun on the level of the spinal cord and in a series of subsequent studies he systematically worked his way up, so to speak. In these studies Hans Kuypers made the most of the advantages of the Nauta method and later of tracer methods using axonal transport, which were developed in the late 1960s and early 1970s (*vide infra*).

He firmly established that there are two descending brainstem systems, terminating in the intermediate zone of the spinal ventral horns: a *medial brainstem pathway* ending mainly in the ventromedial parts of the spinal intermediate zone bilaterally, which are mostly connected to motoneurons of axial and of proximal limbgirdle muscles; and a *lateral brainstem pathway* (for the greater part consisting of the rubrospinal tract), terminating in the dorsolateral part of the intermediate zone from where fibres reach motoneurons of limb and distal extremity muscles, mainly contralaterally. These anatomical data suggest that the medial pathway primarily subserves the guidance of axial and proximal extremity movements bilaterally, and that the lateral pathway is mainly concerned with distal movements and this only contralaterally. In addition to the fibres from these (*subcortical) brainstem pathways* to the spinal motor apparatus there were of course the already well-established *cortical* connections to the spinal cord. These *corticospinal fibres* appeared to be distributed to the same areas of the spinal intermediate zone, as are the brainstem pathways: to the dorsolateral part contralaterally, but bilaterally to the ventromedial parts. Moreover, in the monkey direct corticomotoneuron connections exist, making direct monosynaptic connections with motoneurons of distal extremity muscles (summaries in Kuypers 1981 and Kuypers 1982). These direct cortico-motoneuronal connections are found especially in primates with the capacity to execute independent skilful hand and finger movements. These direct connections do not exist, for example, in the cat and are not yet developed in the infant monkey, which is not yet able to move its fingers independently (Kuypers 1962).

These studies, initiated in Maryland, were continued in Cleveland where Kuypers was appointed Associate Professor in the Anatomy department of Western Reserve University in 1962. He now had a family with four young children and "was by now a well-established figure, recognised as an authority on the Nauta method, which many neuroanatomists in the United States considered as extremely difficult to use" (Phillips and Guillery 1992). In Cleveland, and together with Don Lawrence, a neurology resident, he set up a series of investigations into the functional correlates of his anatomical observations.

In the monkey, the descending tracts were transsected each separately or in combination. When the corticospinal (pyramidal) tracts were interrupted bilaterally, the animals were still able to make a whole range of movements after recovery: they could walk, run, climb, jump, and grasp branches and food morsels, but they could not make relatively independent finger movements. They could not, for instance, extract morsels of food out of a small well with their index finger, and this motor deficit persisted throughout the rest of their lives. In another set of experiments, the lateral brainstem pathways and in still others the medial brainstem tracts were interrupted in already pyramidotomized animals. As expected, these experiments showed that the ventromedial brainstem pathways subserve the regulation of whole body and integrated limb-body movements as well as maintaining posture, whereas the lateral brainstem pathway provides the capacity for individual extremity movements, especially of its distal parts. Moreover, the corticospinal tract, and in particular the direct corticomotoneuronal pathway, appeared indispensible for the execution of highly skilled and relatively independent hand and finger movements (Lawrence and Kuypers 1968a,b).

Being interested in the *guidance* of movement, in particular of distal hand and finger movements, which occurs either by way of somatosensory or by way of visual stimuli, Kuypers had also turned his attention to the cortico-cortical connections from visual and somatosensory cortices to the frontal cortical areas concerned with movement. He had already started these studies in Maryland with Mortimer Mishkin, and they were later elaborated in Cleveland with Deepak Pandya. Taken together these studies showed that the fibres from many other parts of the cortex, in particular from 'visual' cortical areas, converge in the premotor cortex and project from there 'back' to the primary motor cortex from where the direct corticomotoneuronal tract originates (Pandya and Kuypers 1969).

THE YEARS IN ROTTERDAM

In 1966, the first Dean of the Rotterdam Medical School, A. Querido, professor of internal medicine, persuaded Hans Kuypers to return to Rotterdam to become professor of Anatomy at the new Medical School (which later, in 1973, merged with other faculties to become the Erasmus University Rotterdam). He was one of a small group of professors, who were asked, "to build a school that would be free of the constraints and traditions of the past" (Phillips and Guillery 1992). Two professors of anatomy were appointed. Kuypers would teach neuroanatomy and the anatomy of the head and neck. The other professor, H. Moll, would be responsible for the anatomy of the rest of the body. Here, within just a few years, Kuypers built up a truly international department with sections in experimental psychology (with David Hopkins from Canada), neurophysiology (with Simon Miller and later Roger Lemon both from the U.K.), and neuroanatomy (with Don Lawrence from Canada). Under their supervision young students and physicians prepared their doctoral theses on parts of the lab's research line as devised mainly by Kuypers.

The earlier studies on the anatomy of movement were extended. In a clever and surgically difficult set of behavioural experiments in split-brain monkeys (in whom all the commissures had been transsected), Cobie Brinkman and Kuypers obtained strong evidence that in the monkey each cerebral hemisphere steers relatively independent finger movements, e.g., leading to a precision grip only contralaterally, while reaching movements of the arm as well as grasping finger movements (power grip movements) can also be guided by the ipsilateral hemisphere (Brinkman and Kuypers 1973). Subsequently with Rob Haaxma and later with the present author, again in split-brain monkeys, the cortico-cortical pathways possibly subserving the visual guidance of relatively independent hand and finger movements were disconnected and the effects were studied. It appeared that the capacity to execute visually guided highly skilled fine hand and finger movements depends on the integrity of the contralateral cortico-cortical occipito-frontal connections, and that the premotor cortex plays an important part in this respect (Haaxma and Kuypers 1975, Moll and Kuypers 1977). Subcortical structures, such as (on the 'visual' side) the superior colliculus or (on the 'motor'side) the ventrolateral thalamic nucleus seemed to play only a minor role in these evolutionary late developed capacities as are the independent finger movements. Later, with Roger Lemon and Moshe Godschalk, the behavioural characteristics of monkey premotor and precentral neurons before and during visually guided hand and finger movements were recorded. Cells in the premotor cortex appeared to respond during the time that the reward was visible but not during the movement itself, while cells in the motor cortex responded only during the actual movement. The logical conclusion emerged that the premotor cortex was concerned "with recording the position of reachable objects, information that could then be transmitted to the motor cortex for execution" (Godschalk et al. 1981, Godschalk et al. 1985, cited in Phillips and Guillery 1992).

After his wife lost her life in a car accident in 1977 Hans Kuypers spent more time on his six children, the youngest being only nine years of age. But in spite of this terrible loss, the flow of papers published by him and his co-workers continued.

From the beginning of his scientific career Hans Kuypers had been fascinated by staining methods and was always trying to improve them. He was quick to embrace new techniques. In particular the techniques that made use of axonal transport, developed in the late 1960s and early 1970s, were promising and he published many anatomical studies on the technique of and the results with the anterograde transport of radioactive labelled aminoacids and later the retrograde transport of the enzyme horseradish peroxidase (Dekker and Kuypers 1975, Kievit and Kuypers 1975). Later, he developed and perfected retrograde double labelling methods with fluorescent markers (Kuypers and Huisman 1984). These methods revolutionised the research in neuroanatomy as they brought faster and more explicit results with new insights into the wiring of the central nervous system.

THE CAMBRIDGE YEARS

During his years in Rotterdam, Kuypers often felt restrained and even opposed by the University's administrative body. So much so that, in 1984, he took the oportunity to move to Cambridge in England where he was appointed professor and chairman of Anatomy. As his youngest daughter was only 16 at the time, she went with him. Despite a serious heart condition – he had suffered a heart attack not long before – "he threw himself energetically into the reorganisation and rejuvenation of the department, being regarded by some as a bull in a china shop" (Phillips and Guillery 1992). Within a short time he had reorganised and extended the department, and modernised the teaching of anatomy with links to the clinic. He now mainly devoted his research to the development of yet another neuroanatomical tracer. This time it was a virus, the herpes simplex virus, which was known to be transported along nerve fibres, but also across synapses (Kuypers and Ugolini 1990). He came close to achieving his ideal, which was to trace the motor system from the muscles or motor nerves all the way back to the cells of origin in the motor cortex. The task was actually more difficult than it had appeared at first sight. Before this work was accomplished Hans Kuypers died in his sleep on September 26, 1989, in Cambridge.

The person

Hans Kuypers was a man of strong convictions, determined to reach his goals, obsessed by his desire to clarify the hodology of what Sherrington so aptly called the 'enchanted loom', dedicated to his work, his team and his family (in variable order according to circumstance). He could be stubborn and proud and was not always capable of compromise. He took disappointments and personal blows with much courage. The death of his wife was a very severe blow, leaving him to look after his six children, aged between 9 and 21. I remember vividly his wife's funeral: Kuypers standing at the grave with his six children in line next to him, giving the impression: "I promise you, we'll make it." Many female housekeepers were successively hired and fired, occasionally within weeks, when their work was not entirely to his satisfaction (Paul Kuypers, personal communication).

Kuypers was a hard worker, being nearly always in the lab on Saturdays, and so were we! Asking for a day off came close to an indecent proposal. When he suffered his first heart attack in the early 1980s, he was admitted to the University Hospital Dijkzigt, which is connected to the medical faculty building where he had his lab on the 13th floor. Two or three days later, whilst still admitted, I met him in his pyjamas in the lift on his way to the department. He strived for perfection although he knew its limits and could also suddenly say: okay, this is not perfect but it is good enough. He was invariably willing and available to solve problems and the door of his office was nearly always left open so that everybody of his team, even the youngest technician, felt free to enter with questions or suggestions. The atmosphere of the department in Rotterdam was truly international, the language being a curious mixture of English and Dutch. This was partly since the foreign co-workers did their best to speak some Dutch but also because of the many visitors from abroad, almost on a weekly basis, some staying for their sabbatical and most of whom lectured on their research. I was particularly impressed by the visit of Norman Geschwind (1926-1984) with his elucidating views on the disconnection syndromes in animals and men.

Kuypers often had arguments with the University's administrators. When he told the managing board that he was thinking of leaving for Cambridge if his requirements were not met, he was furious but also utterly surprised when they let him go.

As an eminent professional many prizes and awards came his way, and he was elected by quite a number of professional societies. Already in his student years in Leiden he was recognised as a man of strong leadership, being elected president (praeses) of the Catholic Student Association 'Sanctus Augustinus'. He was an excellent teacher and he was very proud when his students awarded him the teaching prize. He received the Winkler Prize for Neurology of the Netherlands Society of Neurology in 1975, and was awarded the Research Prize of the Dutch Federation of Medical and Biological Societies in 1977. He was elected member of the Royal Dutch Academy of Sciences in 1980. He was one of the founding members of the European Neuroscience Association (ENA) and served as its President in the early 1980s. In 1988 he became a Fellow of the Royal Society.

After his death in Cambridge, his body was returned to the Netherlands, and he was buried next to his wife in Rotterdam. Two "Kuypers Memorial Lectures" were held in London, UK; the first bij Peter Strick from Pittsburgh, the second bij Gert Holstege from Groningen on the emotional motor system. Two workshops of the ENA were held in his remembrance, one in Stockholm in 1990 entitled 'new methods for tracing neuroanatomical connections', and one in Cambridge in 1991 on motor systems.

Acknowledgements

While writing these biographical notes I realised again the privilege I have had of working under Hans Kuypers' supervision. Fortunately I could rely on the personal and biographical records of Lemon (1990) and on the detailed biography by Phillips and Guillery (1992). Eddy Dalm sought for and found the photographical picture. Furthermore, talks and correspondence with Rob Haaxma, Gert Holstege, Dave Hopkins, Paul Kuypers, Roger Lemon and Dick Passingham revived old memories, yielded sometimes unexpected facts or anecdotes, and renewed personal relationships.

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R. Magnus *1873-1927*

24

P. Eling*

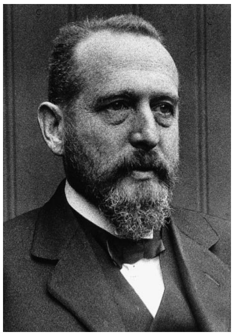

Figure 1.
R. Magnus.

Rudolf Magnus, born on September 2, 1873, was the elder of two children born to the lawyer Otto Magnus and his wife Sophie Magnus Isler. They lived, apparently in fairly wealthy circumstances, in Brunswick (Germany). Diaries from Magnus's mother and grandmother reveal that he was a remarkable child, intensely interested in dissecting his toy animals. Following the Gymnasium, Magnus originally planned to study philology. A friend of the family, professor Richard Meyer, a chemist, convinced him that science would be a far better choice. And so Magnus went to study medicine in Heidelberg in May 1892. Among his teachers figure the physiologist Wilhelm Kühne, the neurologist Wilhelm Erb, Emil Kraepelin for clinical psychiatry, and R. Gottlieb for pharmacology and physiological chemistry. His preserved lecture notes testify to his special interest in neurology. He himself indicated that the lectures and laboratory work with Wilhelm Kühne (1837-1900) were of decisive influence.

Magnus performed his first scientific study under Kühne. It concerned a new method for measuring blood pressure from the exposed carotid artery in animals. This method of direct measurement was also the topic of his first conference paper, which he presented at the 3rd International Physiological Congress in Bern, in 1895. It also was the subject of his doctorate thesis ('Über die Messung des Blutdrucks mit dem Sphygmographen' [On measuring the blood pressure with a sphygmograph]; *summa cum laude*), which he wrote under Kühne's supervision in 1898. Magnus developed a method to record blood pressure directly from the exposed artery, in order to prevent some pitfalls, inherent to other methods, using air or fluid transmission. This was the first of a series of methods introduced or refined by Magnus. Probably the best known of them is the recording of muscle contraction of isolated parts of the feline ileum in a physiological salt solution.

Having completed the medical studies, he went to England for a study trip of approximately five weeks. The main purpose of the journey was to attend the 4th Congress of Physiologists at Cambridge. He also used the opportunity to travel in England and on his way home, he visited Holland. He presented a paper on the neurogenic origin of the pupillary reflex of the eel and the frog. The question was whether the eye's pupillary reaction to light in fish was due to direct sensitivity of the pigmented musculature of the iris, or to the participation of nervous elements in the iris. This latter position was defended by Magnus.

Confronted with the choice between clinical work and science, he opted for the latter. At the end of 1898, he was appointed assistant to his former teacher, Gottlieb (who was married to one of Kühne's daughters), head of the Pharmacological Institute in Heidelberg. He became 'privat Dozent' at the University of Heidelberg in 1900. Being convinced that he had acquired a stable position, Magnus married Gertraud (Traudl) Rau in February 1903. He probably met his wife in Munich where she practiced painting while Magnus was drafted for service in the Bavarian army. Although both came from a liberal Jewish family, they had been baptised a few years earlier. She was an active member of the liberal Protestant community, while Rudolf was not religious. While living in Heidelberg, they had three children: Karl (1903), Margarethe (Gretl, 1905) and Dorothea (Dorle, 1907). Later, while living in Utrecht (the Netherlands), another two children were born, Erika (1909) and Otto (1913).

Magnus was appointed extraordinary professor of pharmacology in Heidelberg in 1904. During the period 1898-1908, Magnus produced over 70 articles on a variety of pharmacological and physiological topics. His early studies had convinced him that an isolated surviving organ can serve as an ideal model to study both its physiology and pharmacology. He considered his studies on the small intestine as the most important of that period. One of the papers concerned pharmacological experiments on the *Sipunculus nudus*, a wormlike animal that had been investigated extensively by his study friend Jakob von Uexküll. The segmental structure of its intestine made, for the first time, examination possible of the effects of different pharmacological agents on the intestinal nervous centres, local nerve reflexes, peristaltic rhythm, and the smooth muscle fibres. He showed that the amount the intestinal muscle layer was stretched determined the direction of stimulus-conduction. At international physiological conferences, he met other scientists, whom he visited at later dates, for instance Schäfer (later: Sharpey- Schäfer), Langley and Sherrington.

Magnus spent seven weeks in Schäfer's laboratory in Edinburgh in 1901, and two series of experiments were carried out. The first one addressed the question whether the vagus nerve contained motor fibres for the spleen. Their experiments on a dog, a cat, a rabbit and a monkey indicated that the answer was negative. The second series of experiments revealed that pituitary extracts produced a rise of blood pressure by contracting the systemic arterioles. Magnus and Langley worked in Cambridge, presumably during the Easter holiday 1905, on movements of the intestine before and after section of the mesenteric nerves. They found that after degeneration of nearly all of the post-ganglionic sympathetic fibres, the Auerbach plexus retained all its functions. Magnus's visit to Sherrington in Liverpool in 1908 turned out to be a decisive experience, as it formed the impetus for his work on postural reflexes, which became the central topic of his research in Utrecht. His goal for that trip was to start research on the question whether a rule, established by his friend von Uexküll for invertebrates, namely that excitation of a nervous centre tends to spread to stretched muscles rather than to relaxed muscles, would be valid for mammals as well.

In addition to physiological work, Magnus, together with his friends von Domaszewski and von Uexküll, became engrossed in Goethe's scientific papers. This is not really surprising, since he originally planned to study literature and admired Goethe. Using Goethe's instruments he replicated his experiments in the Goethehaus in Weimar, especially those on colour perception, although Goethe's other work, e.g., on comparative anatomy and botany impressed as well as inspired Magnus. In a series of ten lectures, published as *Goethe als Naturforscher* (translated as Goethe as a Scientist, 1906), Magnus demonstrated that Goethe's observations were correct, but the conclusions drawn from them were wrong.

On his return from Liverpool, a letter awaited him, confirming his appointment to the chair of 'Pharmacagnosis and Pharmacodynamics' at the faculty of medicine of the University of Utrecht. This was the first professorship to be given in pharmacology in the Netherlands. He accepted the chair with an inaugural lecture on 28 September 1908 on 'Ziele und Aufgaben des pharmakologische Unterrichts' [Objectives and tasks of teaching pharmacology], arguing that its central task is the study of the effects of chemical substances on the organism. Pharmacology, therefore, is closely connected with physiology and experimental pathology, sharing its methodology with physiology.

Initially, the start of World War I did not affect Magnus particularly. The Netherlands remained neutral. However, in 1915 Magnus was called for military service in the German army. At first, he worked as a medical officer in hospitals in Speyer and Mannheim. Later, he was sent to the 'Kaiser Wilhelm Institut' in Berlin, where he investigated, together with Laqueur, the pharmacology of war gases. When the Dutch government informed him that it would have to appoint someone else if Magnus did not return, he obtained permission from the German authorities to return to Utrecht in 1917. He resumed work in the laboratory in a centuries-old building, the 'Leeuwenbergh', together with his co-workers, in particular Adriaan De Kleyn (1883-1949), who cooperated in the experiments on postural reflexes. De Kleyn had studied medicine in Utrecht and settled as oto-rhino-laryngologist there. An essential part of Magnus's experiments involved operations on the labyrinth, and so De Kleyn had become assistant to Magnus in 1912. Their cooperation evolved into a close friendship. Magnus and De Kleyn developed elaborate systems to describe the various postural reflexes. Among these were the Magnus-De Kleyn reflexes, which can also be demonstrated in certain human patients. Experiments were also carried out to investigate the effects of pharmaca on postural reflexes. Other co-workers in this area of research were Willem Storm van Leeuwen (1882-1933), who was involved in several pharmacological studies, and Gijsbertus Rademaker (1887-1957), who worked on a voluntary basis and mainly analysed the involvement of midbrain structures in postural reflexes. Magnus generally wrote the review papers of this work himself. Joannes G. Dusser de Barenne (1885-1940) assisted Magnus, at first on a voluntary basis; later he worked with De Kleyn.

The studies on postural reflexes ('Körperstellung') formed the major part of Magnus's work in Utrecht. Many were published in a series of 24 articles on 'Beiträge zur Pharmakologie der Körperstellung und der Labyrinth Reflexe' [Contributions of Body Posture and Labryinth Reflexes to Pharmacology] and subsequently in the monumental monograph on *Körperstellung* (Body Posture, 1924). A Russian translation of this book appeared in 1962, and an English version in 1987. Magnus summarised the results in the Croonian Lectures, read before the Royal Society in London, 1925.

Magnus also developed other lines of research. One such line was started in Utrecht about 1912, together with his assistant, the chemist Joan Willem le Heux (1881-1950). The latter isolated choline as the chemical substance involved in the occurrence of rhythmic intestinal movements. These studies were summarised in the second Lane lecture at Stanford University, San Francisco on 'choline as an intestinal hormone'. Another series of experiments addressed the effects of digitalis on the dynamics of the heart and blood circulation. A minor topic formed the studies on the pathophysiology and pharmacology of the lungs.

Magnus was also interested in the philosophical background of his work. He adhered to the Kantian framework and believed that we use a number of a priori categories such as time and space to perceive the world. These categories have their basis in physiological processes. This point of view is closely related to Johannes Müller's thesis that the different sensory systems are triggered by specific forms of energies. The fundamental role of space can be observed in changes in eye-position following changes in the position and movements of the head in various animals. Together with De Kleyn, Magnus studied this complicated system (which functions already at a very young age, before the eyes are open) in the rabbit and other mammals. Magnus therefore regarded it as a physiological a priori.

After the war, Magnus' workload increased steadily. He became engaged in the development of materials for teaching pharmacology. He was also involved in the foundation of the 'Rijksinstituut voor Pharmaco-therapeutisch onderzoek' (RIPTO, Governmental Institute for Pharmaco-Therapeutical Research), whose task was to determine the biological standard for drugs that were in use and for the evaluation of new drugs. As a result, he was asked to become a member of a committee for developing an International Standard for Digitalis.

The conditions of his laboratory were not adequate to encompass all these new developments in his work and after a number of unsuccessful attempts to get a new laboratory, Magnus was offered the opportunity to develop plans for a new building. Much time and effort was invested in this project in the period between 1924 and 1927 (see below).

In July 1927 he went to his beloved Pontresina, to prepare the 'Lane Lectures' series for 1928 at the Stanford University. After a walk, he fell ill and in the subsequent night of 24 to 25 July he died, probably due to a cardiac infarction.

Körperstellung (body posture)

Magnus was intrigued by the finding of his friend von Uexküll, that a stimulus on the central nerve ring had a different effect on the muscles of an isolated arm, depending on whether it is in the resting position or bent sidewards. The underlying principle seemed to be that excitation always flows towards the stretched muscles. Magnus realised that this principle might explain the influence of body position on the precise form of a reaction to a stimulus. Moreover, Magnus estimated that Sherrington's experience with the study of reflexes in spinal, decerebrated and mesencephalic animals could be valuable for exploring this issue further. Magnus observed in his first experiments on spinal dogs in Liverpool in 1908, that when the knee jerk reflex was elicited on one side, the effect on the contralateral side depended on whether the leg on that side was bent or extended. Magnus developed a research programme in Utrecht, examining posture in a very systematic way. He distinguished between a static and a dynamic (stato-kinetic reflexes) condition, and examined two kinds of reflex mechanisms, neck reflexes and labyrinth reflexes (otoliths and semicircular canal). He eliminated the influence of each of these by sectioning nerves, centrifugalisation (detaching the otolithic membranes but leaving the canals intact) and by lesioning above or below the thalamus, mesencephalon and the medulla. He used cinematography and stereography to register and document the observed reflexes.

The study of postural reflexes addressed four different issues:

- reflex-standing: muscles sustaining the standing (upright) position should have, by reflex action, a certain degree of enduring tone to prevent the body from falling;
- normal distribution of tone: not just the 'standing muscles' but also the antagonists possess tone, and there should be a balance between these two sets of muscles;
- attitude: the position of different body parts must harmonise with each other;
- righting function: a series of reflexes are evoked to return to a normal position when the body is brought out of the normal resting position.

Magnus maintained that the main centres for these functions are located in the brainstem (fig. 2).

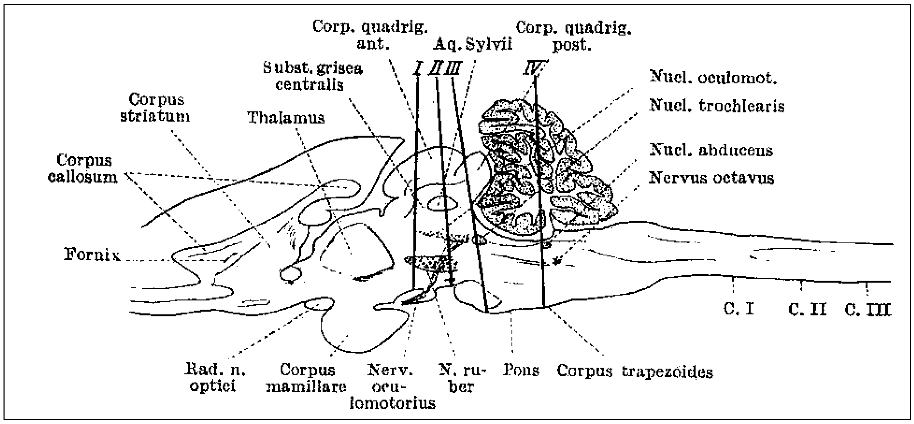

Figure 2. From Magnus: transverse sections in rabbit: different reflexes.

He recommenced studies in dogs, whose thoracic spinal cord had been sectioned. The results did not indicate unequivocally that the intervention produced changes in the central connections, as had been demonstrated in vertebrates. Reflex-sensitivity of the muscles in the hind legs did increase, suggesting some change in sensitivity in the motor centres of the spinal cord. Magnus recorded these reflexes also on film, parts of which were included in a paper, published in 1909. Subsequent studies showed that the results essentially depended on the intactness of the proprioceptive fibres of the ipsilateral muscles.

He subsequently examined decerebrated animals, in which the brain stem had been severed at different levels between the posterior half of the medulla and the anterior half of the mesencephalon. This resulted in the familiar pattern of decerebrated rigidity, in which all extensors are in a permanent state of maximal contraction, while the flexors are relaxed. Experiments, in particular those of Rademaker, demonstrated that the intactness of the red nucleus is essential for the change from decerebrate rigidity to normal distribution of tone, and that the rubrospinal tract carries the impulses down to the spinal cord.

The study of attitudinal reflexes forced Magnus and De Kleyn to discriminate between the influences of the tonic labyrinthine reflexes and the tonic neck reflexes. Neck reflexes could be excluded by cutting the first three posterior (sensory) roots or by bandaging head, neck and thorax. Labyrinthine reflexes were excluded by extirpation of the labyrinth. It appeared that all attitudinal reflexes could be attributed to the cooperation of labyrinthine and neck-reflexes. The general rule was that every group of muscles reacts to the algebraic sum of stimuli arising from the labyrinth and neck receptors, so that if the extensors of one forelimb acquire increased tone from both the labyrinths and the neck, the limb will be strongly extended, whereas if their tone is increased by the labyrinths and decreased from the neck it may remain unchanged.

Righting reflexes cannot be studied in a decerebrate animal. They can best be studied in a mid-brain animal or thalamus animal, in which the forebrain had been removed so that no voluntary corrections are possible. There are various groups of righting reflexes: labyrinthine, body reflexes acting on the head, body reflexes acting on the body and neck righting reflexes. Higher animals such as cats, dogs and monkeys with intact cerebrum show a fifth group, the optical righting reflexes.

Another clear result from the experiments was that these postural reflexes are undisturbed after extirpation of the cerebellum, and therefore the cerebellum does not play a role in body posture.

In a separate chapter of his book, Magnus discussed extensive pharmacological studies on postural reflexes. Different drugs appeared to have considerably different effects on the various reflexes. The final chapter concerned investigations on postural reflexes in newborn animals.

Personality

Rudolf Magnus and his wife Traudl both came from well-educated, cultured, intellectual, liberal Jewish families. He was of small stature and for that reason got the nickname 'Winzig' (Tiny). He felt at home in Utrecht, but kept intensive contacts with relatives and friends in Germany. According to Otto Magnus (2001), the family was harmonious. Traudl took care of the upbringing of children, running the household, the finances and the social activities. After dinner, Magnus went to his study to work and did not want to be disturbed. Like his father, Magnus enjoyed hiking in the mountains and holidays were often spent in the Alps. He also liked figure skating. Detailed reports of his journeys, describing both the surroundings as well as the scientific meetings, were mailed home to his parents as well as his own family. He was a gifted speaker and teacher (Oljenick 1972). His list of publications containing over 300 items not only testifies to his abounding energy, but also reveals his knowledge and insight in wide areas of science. As well as being a first-rate pharmacologist and physiologist, he was anatomist, botanist, philosopher and historian.

The awards he received confirm that his impressive contributions were recognised. In 1919, he was elected as member of the Royal Academy of Sciences in the Netherlands. That same year he received, together with De Kleyn, the Guyot prize from the University of Groningen. In 1925 the Queen of the Netherlands appointed him 'Knight in the Order of the Dutch Lion'. The Royal College of Physicians in London awarded him the Baily Medal in 1925. One year later, he was invited to present the Cameron Prize lectures in Edinburgh. In 1928, posthumously, he received the 'Hans Horst Meyer Medaille für Fortschritte in der Experimental Medizin' [medal for progress made in experimental medicine] from the Austrian Academy of Sciences.

It was not until 1962 that it was revealed that Magnus, together with De Kleyn, had been a serious candidate for the Nobel Prize. In *Nobel, the man and his Prizes* (1962) one can read:

> "The investigations of R. Magnus and A. de Kleyn referred to above concerned tone and posture in different circumstances. It was found that the rigidity developing in decerebrate animals after transsection of the brainstem, especially in their limbs, depends to a large extent on the position of the head. A more detailed analysis revealed that this was a question of tonic reflexes, which were affected partly by the position of the head in space and partly by its position in relation to the neck. Both groups, which can reinforce or weaken each other according to a definite pattern, have been combined under the name of attitudinal or standing reflexes since they enable the animal to stand up. These reflexes can also be observed in normal, intact animals; they play an important part in all habitual movements. While a decerebrate animal can stand up but is not able to get up on its feet, it can get up if the cerebrum alone has been removed, provided the big nerve centres or ganglia situated at the base of the brain are left intact. This ability is due, as Magnus and De Kleyn discovered, to a special group of 'righting reflexes', which are elicited, partly by the vestibular apparatus in the inner ear, and the neck, partly by the eyes, and, partly, by the trunk of the body. It is these complex reflexes, which enable a cat always to land on its feet. Obviously, they are also of the utmost importance in man."

The works of Magnus and De Kleyn were declared by the examiner (1927) to clearly deserve a prize, and the prospects for an award seemed most favourable when Magnus died.

The Rudolf Magnus Institute

Magnus's first laboratory was housed in 'Leeuwenbergh', a church-like building, founded in 1567 as a hospice for plague victims. The founder of Dutch chemistry, Gerrit Jan Mulder had used it for his laboratory in the 19th century. In view of the cramped conditions in Heidelberg, Magnus was happy with this institute. Many of the experiments on body posture and practically all of the photography were done in the open air in the courtyard.

Magnus wrote a letter to the board of trustees in 1917, indicating that the Institute had become entirely inadequate and he requested new equipment. Repeated requests over a number of years remained unsuccessful. When Magnus was offered the chair of the physiologist Hamburger in Groningen, where a new laboratory had been built twelve years before, he seriously considered moving. Magnus was also offered the chair of Pharmacology in his Alma Mater in Heidelberg about 1924. The dean of the faculty immediately brought this to the attention of the trustees and, with the help of the Medical Education Division of the Rockefeller Foundation in New York and the Dutch government, the university decided to found a new pharmacological laboratory. This fact may have played an important role in Magnus's decision to decline the invitation from Heidelberg.

The cornerstone of the new Institute Nieuw Leeuwenberg was laid in 1926. It was opened in the autumn of 1927, but because of his sudden death Magnus never saw the completion of his new institute. His successor, Ulbe Bijlsma (1892-1977), inaugurated it in 1928 and headed the institute until 1954. In 1963 David de Wied (b. 1925) was called from Groningen to take over the chair of Pharmacology. He arranged for the Institute to be named the 'Rudolf Magnus Institute' (RMI) at the occasion of its founding 60 years ago. At a special ceremony, Magnus's grandson Jan R. Magnus unveiled a commemorative stone in the façade of the building. The RMI moved to the new university campus at the outskirts of Utrecht, the 'Uithof' in 1994.

Note

* The author gratefully acknowledges the assistance of Dr. Otto Magnus, who provided him first with a 1995 paper on Rudolf Magnus, and later with an entire monograph: Rudolf Magnus: physiologist and pharmacologist (2002). The current biography is based primarily on this material.

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Körperstellung. (Integral translation into Russian by Uskanovkatela). Published by the Academy of Sciences of the U.S.S.R.

G.G.J. Rademaker *1887-1957* 25

L.A.H. Hogenhuis

Figure 1.
G.G.J. Rademaker.

Gysbertus Godefriedus Johannes Rademaker was born in The Hague on March 19, 1887 as a son of the minister of the Dutch Reformed Church Geurt Arend Rademaker and his second wife Safke Maria Louize Dorothea Notten. He studied medicine at Leiden, graduating in 1912 after having completed his surgical training at the 'Zuidwal' Municipal Hospital in The Hague. When his brother (who was a general practitioner in Surabaja in the Dutch East Indies) fell ill, Rademaker went out to act as *locum tenens*. He stayed and established his own practice. After working there from 1916 till 1922 as a GP and general surgeon, he returned to the Netherlands leaving behind a practice that has been called "the largest in the Dutch East Indies." Family circumstances compelled him to return to Holland without fixed plans as to his further activities.

Three factors determined his ultimate choice of career: his *peregrinationes academicae* to important clinical centres and laboratories in London, Paris and Berlin; the awakening of his interest in scientific work; the advances in neurophysiology made by Sherrington, and Rademaker's introduction to Magnus, Professor of Pharmacology at Utrecht, who was a good friend of Sherringtons and one of the great neurophysiological thinkers of his day. In 1922, Rademaker joined the group that had been working in Magnus's laboratory since 1912 to develop Magnus's concept of 'Körperstellung' (body posture) - a brilliant neurophysiological analysis of the activities of walking and standing. According to Ter Braak et al. (1953), "Next to Sherrington and Pavlov, Magnus must be named as one of the great promotors of a mechanistic conception of the function of the central nervous system. He had evolved the view that 'normal' body posture is based on an equilibrium of reflex muscular contractions and, together with his collaborators, he had set himself the task to analyse the individual reflexes contributing towards this equilibrium, to trace the receptors involved and to delimit the central nervous pathways. In the course of these examinations the great significance of the midbrain had gradually been brought to light and it fell to Rademaker to verify this view and to define it more precisely."

Thanks to his surgical past, Rademaker proved to be highly skilled in operating on experimental animals. In particular, unlike others – including Magnus – he developed a delicate technique for operations at the level of the mesencephalon and cerebellum, which (combined with effective postoperative care in which, as we shall see below, his wife played an indispensable part) would guarantee the animals concerned a long postoperative life.

To cite Magnus from his Cameron Prize Lecture delivered at the University of Edinburgh on 19th and 20th May 1926[1] in which he summarised, a year before his death, "Some results of studies in the physiology of posture - commenting on local static reactions":

> "The limbs of mammals, as of other vertebrates, are built up of bony segments, linked by a complicated arrangement of ligaments and moved and fixed by muscles; fasciae also play a role. The whole system is easy movable in different directions. Our problem is to explain how such a movable limb is at times used as an instrument for very different purposes (such as scraping, scratching, fighting, etc.) and moved freely in all joints, whereas at other times it is transformed into a stiff and strong pillar which gives the impression of being one solid column, able to carry the weight of the body. Experiments have shown that this is accomplished by a series of local static reflexes.
>
> We were confronted in the laboratory with this problem during the investigation of decerebellated animals, which had been operated upon by Dr G.G.J. Rademaker, and of which the condition of muscle tone had to be followed during the course of many months. It soon became evident that this was not a simple task, and that the state of tone of a limb at any given moment depended greatly upon the way in which the tone is investigated. If, for instance, a dog is lying down in the lateral position and the resistance of one forelimb against passive flexion is measured with the hand and fingers flexed, often no resistance can be felt. But if the latter are extended and pressure exerted against the pads of the foot, then the forelimbs become strongly extended and can hardly be flexed at all. The same difference can be demonstrated in intact animals. We therefore decided to make a more detailed investigation of these reactions."

Owing to his remarkable talent for unprejudiced analysis of the behaviour of experimental animals as well as to his above-mentioned operative skills, Rademaker turned out to be and undoubtedly was the right man for such an investigation. His first research project involved the infliction of lesions in or near the midbrain, the analysis of the changes in the reflex behaviour, tone and motricity of the extremities produced by these lesions and finally the microscopic-anatomical investigation of material from the experimental animal, after preliminary study of the detailed anatomy of the brainstem with Winkler. He inferred from his experiments that the red nucleus should be considered the principal centre of the labyrinthine and righting reflexes, which were found to be indispensable for a normal distribution of muscle tone. A great many other inferences were drawn regarding the localisation of reflexes pathways which did not involve the red nucleus. Rademaker's doctoral thesis (1924) in which the results of these investigations were laid down was bore the title: *The significance of the red nuclei and other parts of the mesencephalon for muscle tone, body posture and labyrinthine reflexes*. Completed in the remarkably short space of time of two years, this study made a deep impression of the medical world of the time, since "it assigned for the first time on the ground of exact experimental research a function to a delimited nuclear area in the brainstem whose anatomical connections in themselves gave no direct indication of this function" (Ter Braak et al. 1953).[2] Rademaker's working method proved to be innovative. He drew a significant distinction between acute and chronic experiments, which allowed greater precision about the location of the lesion to be inflicted and helped to clear up the massive confusion associated with the 'decerebrate rigidity' model, widely used at that time (e.g., in Sherrington's laboratory). His thesis was approved *cum laude* at the University of Utrecht, and was translated into many languages (e.g., into German under the title *Die Bedeutung der roten Kerne* in 1926). Subsequent investigators, reviewed by Fulton (1943)[3] "showed that the question is more complex; the red nucleus is but one of a series of levels of elaboration of the righting reflexes.... Rademaker's monograph nevertheless greatly clarified the issues" (Denny-Brown 1980).

In 1928, Rademaker was nominated as successor of the Nobel laureate Einthoven (1860-1927, inventor of the string-galvanometer 1903, by means of which he produced the first electrocardiograms 1906), to the chair of Physiology in Leiden. He remained in this position until 1942.

His students liked his style of teaching[4] – especially the demonstrations, when he used postoperative findings to elucidate the underlying neurophysiology. During his lectures Rademaker, with his leptosome build, impeccably tailor-made suit, knife-edge creases in his trousers, and highly polished shoes, was the very model of the English gentleman or 'le gentilhomme' in the sense given in Larousse: "homme qui fait preuve de délicatesse dans sa conduite." He let no opportunity slip to express his admiration for Sherrington or similar eminent scientists, and to cite their works. Illustrations show him either working in the laboratory in a messy lab coat or adjusting some piece of scientific equipment in the same laboratory or an animal house, dressed in a three-piece blue tailor-made suit. Cartoons of him circulated in student circles.

In the tradition of the reflexological approach, which dated back to Descartes, was further developed on the basis of the experimental work started by Sechenov (1829-1905) and continued up to the work by the 30-year younger Pavlov (1849-1936), who succeeded Sechenov in the St. Petersburg chair of Physiology, Rademaker set up a new programme of experimental work. He aimed to explain the blink reflex in response to threatening movements on the basis of new data obtained from study of the 'big decerebrate dog', e.g., by Goltz (1834-1902) in Strasbourg and other workers in various German laboratories. Rademaker succeeded in revealing the mechanism of this reflex, using ingenious techniques for ablation of parts of the cerebrum (in cooperation with Gelderblom[5] and later with Ter Braak), and to show the clinical relevance of this study later, in cooperation with Garcin at the Salpêtrière in Paris. This was the first experimentally based, neurophysiological and clinical demonstration of a cortical/subcortical reflex – a matter that was attracting a great deal of interest in the neurological world. This method of examination yielded what became known as the 'Rademaker-Garcin sign' in the neurological clinic (i.e., the blinking reflex to threatening movements).[6,7]

During his early years as professor of Physiology in Leiden, Rademaker completed his second monograph, *Das Stehen* [On Standing], which summarised the results of his extensive programme of experiments and parts of his clinical work (1931). This work was primarily an analysis of cerebellar defect but with much wider significance in relation to the neurological mechanisms of righting, standing and equilibrium. Rademaker devised ingenious clinical tests to investigate the exact nature of the complex abnormalities of posture and movement that had hitherto been loosely categorised as 'incoordination', 'asthenia', 'dyssynergia' and 'atonia' (Denny-Brown 1980).[8] Some of the basic reactions that Rademaker established, such as 'placing' and 'hopping', have become well known to physiologists and clinicians. "That the cerebellum is not in fact an essential part of the mechanism of any of the labyrinthine reactions was an extraordinary finding" (Denny-Brown 1980). Physiologists all over the world – but particularly in the United Kingdom, United States, France and Germany – recognised the work as a classic. "The complete objectivity that Rademaker achieved gives them a timeless quality that also distinguished the investigations of Gordon Holmes on the human cerebellar syndrome ten years earlier" wrote Denny-Brown in his foreword to the English translation of the original German text of *Das Stehen*.

The earlier work of Magnus and de Kleyn, that had focused mainly on peripheral mechanisms and reflex patterns associated with posture, standing and walking, was now supplemented by Rademaker's findings obtained during experiments focused on central mechanisms. *Das Stehen* was a monumental work, and constituted Rademaker's manifesto.

His third monograph, *Réactions labyrinthiques et équilibre* [Labyrinthine reactions and equilibrium], was published in 1933. It contained the results of a logical sequence of studies of equilibrium reactions in experimental situations and clinical practice, with an impressive series of deductions from premises, some of which were based on a series of photographs of the various positions of the head in space taken previously from different points of the compass ranging from 0 to 360° coupled with the results of tests performed at the different positions.

The experimental results, which had a direct bearing on clinical practice, attracted a great deal of interest at the time. The tests making use of a tilt table, which Rademaker developed in association with his friend Garcin in Paris, became widely known in the world of French neurology. The text of this monograph was full of new ideas, but never received much attention outside the French-speaking world because an English version was never published. As was pointed out in the book itself, *Réactions labyrinthiques et équilibre* was intended as a follow-up to his previous monograph *Das Stehen*. Guillain (1876-1961) wrote a very useful introduction to the book, recommending it to a wide audience of physiologists, neurologists and otologists.

When Rademaker arrived in Leiden in 1928 to take up his position as professor of Physiology, he encountered a situation whereby neurology lectures were read by the professor of Psychiatry, Jelgersma (1859-1942), when the occasion arose. Jelgersma also looked after neurological patients in the department of Psychiatry, where he was assisted for a number of years by the lecturer A. Gans, whose lectures apparently were not overly appreciated by the students.

It was not until Rademaker was made professor of Neurology in 1945, just after the end of World War II, that effective steps were taken to separate the disciplines of psychiatry and neurology at Leiden. Indeed this, including the setting up of the Institute of Neurology at the university, was Rademaker's main task during the early years of his new professorship. He was guided during this process of change by the conviction that the relationship between (neuro) physiology and neurology was more important than the one between psychiatry and neurology, which had received the main stress in the past. After the war years, Rademaker continued to contribute papers on subjects such as lengthening reactions (1947), visual placing and optokinetic reactions (1948), and clinical discussions of ataxia, nystagmus and related subjects.

Research and other activities came to a complete halt in Leiden during the years of the Second World War. The University was closed by the Germans when it protested at the sacking of the Jewish professors at the University that had been ordered by the occupying forces. Rademaker adopted an active resistance stance, and took part in underground activities during these years. These activities included the setting up of a resistance cell (with its own printing press, weapons-cache and sickbay in his laboratory and the adjoining basement). Students, Jewish and others, admired him for his courage in helping them to continue their studies while in hiding. He visited them there regularly, often unexpectedly, popping up like a Scarlet Pimpernel, being transported to their address by the undertaker in his hearse to keep out of sight of the occupying forces or collaborators. These activities were good for a number of anecdotes that circulated among the population of Leiden, helping to keep up their spirits during the dark days of the Nazi occupation.

Rademaker the man had many faces. In Leiden, he was seen mainly as an introverted, unaffected scientist with high ethical standards. American neurophysiologists (such as John Fulton and Derek Denny-Brown) knew him as the 'king of the red nucleus'; French neurologists as the *prestidigateur* (the magician); English neurophysiologists as the 'microsurgeon with the golden hand'; his students as the inspired 'performer'; and his Dutch colleagues apart from the above epithets as the 'film-maker' who loved to record all details of his experiment – including himself – for subsequent showing on the silver screen (the complete film archives seem subsequently to have been mysteriously lost – possibly destroyed in view of the fire hazard which they were thought to represent). His 'French connection' was often mentioned. This referred in the first place to his wife Maria Josephina Wenceslase Stoltz (Blanche), who came from French Alsace and who literally became his first assistant, in the basement of their apartment in Utrecht, caring for the animals on which he had operated. Her devoted care was crucial for the long-term post-operative survival of these animals, which played a key role in Rademaker's experimental success. Rademaker was a great believer in the education of women, at a time when this was less self-evident than today. They had no children. Among his closest friends were Winkler, Ter Braak, Verbiest, Gorter and Barge.

His fellow professors and university staff knew him as the well-balanced administrator with high ethical standards, always prepared to listen when differences of opinion arose between colleagues. Finally, after the war years, he became the *eminence grise*, the man with the authority to carry out the most difficult tasks such as completing the 'plan Cité Médicale' for the Academic Hospital in Leiden in 1945, where the Physiology department and the newly built Neurology department occupied a central place. He was always marked by great objectivity, a sense of humour and the courage to tackle any problem.

Rademaker's first disciples come from his period as professor of Physiology at Leiden. The seeds he sowed bore rich fruit in many, such as the brilliant Ter Braak, later professor of Clinical Neurology in Rotterdam, his 'favourite son' Storm van Leeuwen, later professor of Neurophysiology at Leiden and Utrecht, Verbiest, the first professor of Neurosurgery at Utrecht, and finally Luyendijk, the first professor of Neurosurgery at Leiden. His pupil L.J. Endtz – greatly admired by Rademaker and others – later headed the prestigious department of Neurology in the Leyenburg teaching hospital in The Hague.

Among his followers abroad may be counted Derek Denny-Brown from Harvard and John Fulton from Yale in the United States, and Georges Guillain and Raymond Garcin from the Salpêtrière in Paris. They have borne witness in both speech and written word to his importance for their eminent contributions to neurophysiology and neurology.

In more recent years, Berthoz (1998) has expressed renewed interest in the results of Rademaker's experimental work and the concepts he used in the study of labyrinthine reactions and equilibrium, which are now found to be applicable to key issues in space neurology.

Rademaker was a major scientist who changed our perception of neurology and in particular the approach taken to posture and motor development. He trained a new

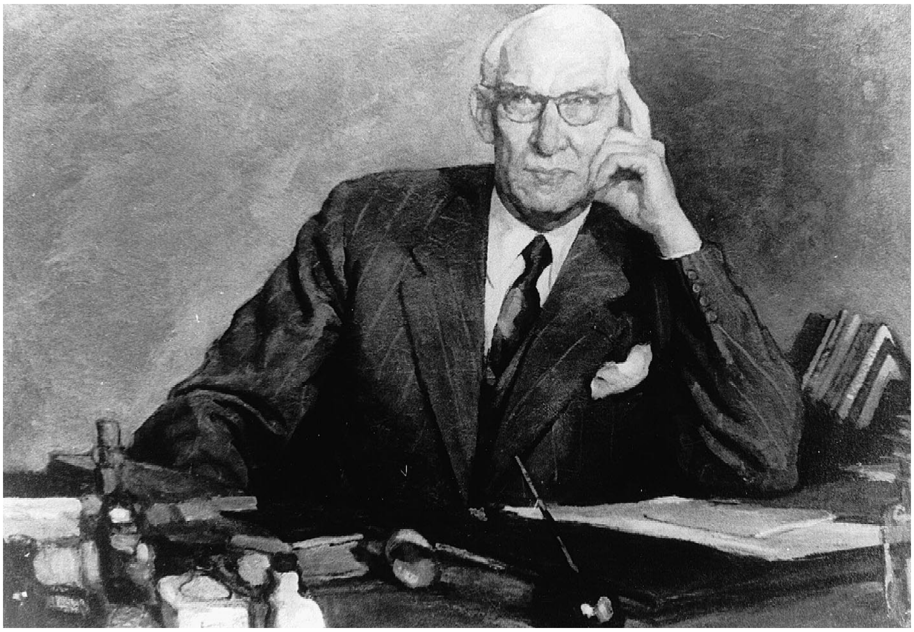

Figure 2. Prof. G.G.J. Rademaker (1887-1957).
The painting, currently hanging in the conference room of the neurology clinic in Leiden, was presented to him by his colleagues and pupils on the occasion of his 70th birthday.

generation of neurologists (including the author of the present review). His publications (73) remain relevant. In view of all his contributions, his fame is hardly surprising. He received many decorations: Member of the Royal Academy of Sciences in the Netherlands, he was an honoured representative of the Dutch scientific world at congresses abroad; he was promoted to the rank of "*Officier of the Légion d'Honneur,*" and elected member of the *Leopoldino* order in Halle, Germany.

Notes

1 Magnus, R.: Some results of studies in physiology of posture. Cameron Prize Lectures. Lancet ii (1926) 531-536; 585-588.

2 Ter Braak, J.W.G., W. Storm van Leeuwen and H. Verbiest: Miscellenea medica in honorem viri clarissimi, Gysberti Godefridi Ioannis Rademaker (with incomplete list of publications), Folia Psychiatr. Neurol. Neurochir. Neerl. 56 (1953) 393-565. Festschrift on the occasion of his silver jubilee as professor at Leiden.

3 Fulton J.F.: Physiology of the Nervous System. 2nd edition. New York, Oxford Univ. Press (1943).

4 ten Cate J., C.U. Ariëns Kappers, G.G.J. Rademaker and G. van Rijnberk: Nederlandsch Leerboek der Physiologie. Vijfde deel., tweede herziene en vermeerderde en van een register voorziene druk. Amsterdam, C.V. Swets & Zeitlinger (1944).
The chapters Physiology of the cerebellum (147-215), The brainstem (234-277) and The cerebrum (277-335) were written by Rademaker, and remained standard teaching texts for many years.

5 Rademaker, G.G.J. and J.J. Gelderblom: Der zentrale Mechanismus des Blinzelreflexes auf Drohbewegungen. Proc. Kon. Acad. Wetenschappen 33, nr. 10 (1930)

6 Rademaker, G.G.J. and R. Garcin: Le réflexe de clignement à la menace. Sa valeur diagnostique dans les lésions corticales et occipito-rolandiques des hémispères cérébraux. C.R. Soc. Biol. Paris (1932) 547-550.

7 Rademaker, G.G.J. and R. Garcin: Le réflexe de clignement à la menace (étude physiologique et clinique); la valeur sémeiologique de son abolition dans les lésions corticales rolandiques et occipito-rolandiques des hémisphères en l'absence de toute hémianopsie. Encéphale 29 (1934) 1-17.

8 Denny-Brown, D.: Foreword to 'The physiology of standing; postural reactions and equilibrium with special reference to the behavior of decerebellate animals' by G.G.J. Rademaker, Minneapolis, University of Minnesota Press (1980) V-VII.

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H.W. Stenvers *1889-1973* 26

J.W. Stenvers

Figure 1. Hendrik Willem Stenvers.

Hendrik Willem Stenvers was born February 16, 1889, in Deventer. He died August 26, 1973 in Zeist. He was my grandfather's brother and therefore my great-uncle. As a child he developed sepsis following a small pox vaccination. This infection was followed by otitis media, resulting in hearing loss. As a consequence his achievements at preparatory school were below level. A tonsillectomy (at that time a major surgical procedure) was performed at the age of ten and, following it, his mental achievements greatly improved. This experience made a great impression on the young Stenvers and probably influenced his later choice to study medicine.

After finishing the 'Higher Burgher School' in Deventer he enrolled at the University of Utrecht in 1907. His entire active life was spent in Utrecht. During his student years his interests were not restricted to medicine. For instance, he also attended lectures of Bolland, Professor of Philosophy at Leiden. This Hegelian philosopher considered pure reason as the expression of truth – a way of thinking that governed the life of my great-uncle. (Bolland's favourite expression was that statements ought to be made only after "they had passed through the 'Holy Halls of Pure Thinking'").

Stenvers graduated on October 13, 1913. Three days later he started as assistant of professor Heilbronner, at the time head of the psychiatric-neurological university clinic in Utrecht and known on the continent for his work on aphasia. As a result of his philosophical studies Stenvers was interested in human conscience and thought; hence his choice for training in psychiatry and neurology. As early as the beginning of 1914 Stenvers was put in charge of the clinic's Röntgen department. He had to make and develop the roentgenograms himself and continued to do this until late in his life. In 1964 my father, who was also a neurologist, was given my great-uncle's last Röntgen apparatus.

Professor Heilbronner died suddenly in 1914. Despite the short training-period, my great-uncle spoke of Heilbronner with much respect all his life. My great-aunt was an intimate friend of Mrs. Heilbronner. Heilbronner was succeeded by professor Winkler in February 1915, whose influence of careful anatomical observations can be recognised in many of Stenvers' papers. Stenvers also collaborated closely with Magnus and De Kleyn. He tried to transform the experimental neurophysiology of those days (consisting of detailed analyses of posture and postural reflexes) to clinical symptoms. During World War I, Stenvers was called to active military duty and stationed as an army doctor, first at Blerick (near Venlo) and later at Jutphaas (near Utrecht). As a consequence, he also could fulfil his academic duties in Utrecht.

In 1917, he married Miss M.C.A. van der Laan. She had graduated as a pharmacist at the University of Utrecht. Although she was an independent woman with broad cultural interests she faithfully supported my great-uncle all his life. Their marriage remained childless. In my memory they were elderly people and not very used to youngsters. They exhibited a great erudition and liked to cite Goethe often, but they were not haughty and were always interested in other people. The stately house at the Maliebaan in Utrecht, where they lived for many years, gave the impression of scientific discipline as well as of harmony. When I stayed with them overnight in 1965, they still had a living-in servant. In the dining room, dinner was served when my great-aunt rang for it.

During World War I, Stenvers published more than a dozen articles, mainly on the subject of cranial röntgenology and its significance for the clinician. In this period he developed the 'Stenvers projection' of the petrosal bone (Stenvers 1916, 1917). Until the beginning of the 1970s, this technique was standard whenever a pontine-angle tumor was suspected. These studies earned him eponymous fame, but he considered this technique mainly as a skill. He regarded his later work – essentially about (un)conditioned cerebral reflexes – to be more important.

In 1920, Stenvers defended his thesis on 'Clinical study of the cerebellar function and the diagnosis of cerebellar and pontine-angle-tumors', in which he stressed the importance of X-ray examination of the petrosal bone (Stenvers 1920). He preferred the term pontine-angle tumor to the one of acoustic neurinoma. Cerebellar dysarthria may be present in unilateral cerebellar lesions; in this case the cerebellar lesion is localised in the cerebellar hemisphere contralateral to the dominant cerebral hemisphere (in a right-handed person, therefore, in the right cerebellar hemisphere). Stenvers did not consider the cerebellum as a centre of coordination, but as a reflex organ regulating voluntary movements learned by practice (cycling, swimming, playing the piano, etc.).

Bárány's lecture, during his visit to Utrecht in 1922, on 'Railway-nystagmus' evoked Stenvers' interest in optokinetic nystagmus (OKN). In 1924, 1926 and 1935, Stenvers published papers on this subject based upon ten cases, carefully controlled by surgical intervention and autopsy. He discovered that in the case of optic tract-hemianopsia the OKN is normal to both sides, whereas in the case of hemianopsia caused by a lesion of a cerebral hemisphere the OKN is absent to the hemianopic side. This means that the cerebral reflex to both sides remains preserved, even when optic impulses do not arrive in one hemisphere. An occipitofrontal pathway is responsible for the fast component of the OKN; the gyrus angularis subserves the slow component.

By means of similar investigations, Stenvers attempted to make what was known at that time as the 'silent zones' of the brain (mainly the right hemisphere) accessible for examination.

Stenvers' visit to Von Monakow in Zürich (1922) revived his interest in aphasia. Von Monakow advised him to discard everything that had been written so far on the subject and to start afresh. In his 1923 paper on "so-called aphasia, alexia and agraphia," Stenvers' philosophical approach led him to make statements such as "there is no man who has ever made a thought himself. The construction and development of our thoughts occurs as unconsciously as the chemical anabolic processes of our body. The possibility that our thoughts can be influenced should not seduce us to decide that we indeed can make thoughts. The forming of thoughts happens automatically."

Disturbances of speech, reading and writing are usually named after the deficit. Stenvers proposed to start from the principle of cerebral reflexes. A disturbance should not simply be considered as the result of a localised cerebral lesion but as the result of a disturbed reflex loop.

In later years, his interest was mainly optico-motor reactions, though he also regularly wrote about the significance of radiology for neurology. For instance, in 1928 he published a monograph titled 'Röntgenologie des Felsenbeines und des bitemporalen Schädelbildes' [Roentgenology of the petrous bone and of the bi-temporal skull]. In the renowned *Handbook of Neurology* (Bumke und Foerster 1936) he wrote two chapters, one concerning 'Radiology' and the other 'Posture and support reflexes, support reaction' (Stenvers 1936a,b).

Winkler retired in 1925. As a consequence Stenvers chose to leave the University Clinic, much to his regret, and established a private practice in the Deaconess' Hospital in Utrecht. He did his clinical and his scientific work more or less alone, in the hospital or at home, consistently and faithfully sustained by the deaconesses. Even after his retirement they visited him and helped him until he died.

His studies on optic motor reactions led to several reports and ultimately to a monograph (*Les Réactions Opto-motrices*) published in 1961 when he was 72 years old. In the monograph four phenomena are closely analysed, namely the OKN, the menace-reflex, the capacity to locate objects by grasping in the field of vision with the ipsilateral as well as with the contralateral hand (direct localisation), and the capacity to locate objects by image in a hemianopic field of vision (localisation by imagination). When examining the direct localisation the investigator stands behind the patient who is looking straight ahead. The patient is instructed to grasp an object in the peripheral field of vision. In hemianopic patients localisation by imagination can be investigated by placing an object in the intact field of vision. The patient is then asked to localise the subject in the hemianopic field of vision. Localisation by imagination can also be investigated in patients with intact fields of vision. One simply asks the patient to close his eyes. The direct localisation can be disturbed in occipital, parietal and frontal lesions. Localisation by imagination is normal when both occipital poles and a connection between them through the callosal splenium are intact. In the case of tractus hemianopia localisation by imagination is intact on both sides.

Examination of optico-motor reactions has nowadays more or less fallen into oblivion, as has the examination of colour and form recognition in the fields of vision, an established part of the examination Stenvers recommended (Stenvers 1955).

Another returning theme in his work was the analysis of various forms of pain. He was especially interested in 'psychalgia'; pain without demonstrable origin, usually considered as psychogenic. He proposed the term 'cerebralgia'. In accordance with his ideas on the visual system he thought that cerebralgias should be considered as conditioned cerebral reflexes. In an article published in 1954 he wrote the following about the treatment:

> "When a patient suffering from often intensive pain seeks medical advice, patience and time are the primary requirements on the part of the practitioner. The first examination requires an average of 90 minutes. History-taking should be detailed and complete, covering not only the pain per se (its localisation, nature, mode of occurrence, etc.), but the entire personality and the conflicts to which it is subject [...] History-taking, even when it seems to warrant a tentative conclusion, must be followed by a complete physical examination with a view to discovering the cause of the pain. This point is of sufficient importance to justify the emphasis with which it is mentioned, firstly because it may be difficult to detect the cause (this may require the use of all possible diagnostic aids) and secondly because a complete physical examination is of importance with a view to the further course of treatment and as an aid in establishing the necessary atmosphere of mutual confidence between the patient and the practitioner. The practitioner is always confronted with an element of uncertainty, as he knows (or should know) his own limitations. The patient, however, may be given a feeling of security in this manner: he will understand that everything possible is being done for him. It has always been my custom to have the patient indicate on a chart the localisation of his pains. This localisation often supplies valuable information regarding the nature of the pain, provided the practitioner is completely familiar with the peripheral and segmental distribution of sensitivity over the body and is informed about Head's 'referred pains' and their typical localisations [...] The next important part is the detection, in the history, of inter-relationships between the pain and certain conditions of tension associated with anxiety and fear. The circumstances attending the first attack of pain are of great importance in this respect" (Stenvers 1954).

These insights are still valid today.

Almost all his life Stenvers was scientifically active. His mind ranged over many different subjects. For instance, he described the first Cryptococcal infection of the nervous system in the Netherlands (Stenvers 1934). He published several articles on the relation between neurology and neurosurgery. One article dealt with the position of the head in tumours above and below the tentorium. In supratentorial tumours the head has a retroflexed position and in posterior fossa tumuors the head is flexed. Stenvers thought that the head adopts a position that facilitates the outflow of cerebrospinal fluid (Stenvers 1925).

He also had strong opinions about psychiatry. He considered this discipline a pure natural science. His article on 'Hysteria and reflexes' (1935) is still worth reading.

For most of his life my great-uncle did his scientific work alone. He therefore made no school: he was a school himself. Owing to politico-religious reasons (a catholic professor was preferred above a Mennonite) he never got the chair he deserved. A citation index search showed that his name is mentioned still, mainly in historical reviews concerning radiology. On the occasion of his 70th birthday a 'Stenvers volume' was published (1959). For this volume his close friend Verbiest, professor of neurosurgery in Utrecht, wrote a biography (Verbiest 1959). Ten years later Verbiest published a shortened version (Verbiest 1969).

About one year before his death my great-uncle had to move to a retirement home. A few days before the move he had a stroke with a serious aphasia. It was sad he had to live through this experience himself.

To conclude this biography I would like to mention that my great-uncle played an active role in the resistance movement during World War II. As a token, he received a medal with the inscription "Alleen een vrij man kan een goed geneesheer zijn" (only a free man can be a good physician). He was a good physician all his life. He was also the last of a generation of neurologists who tried to localise a lesion in the nervous system by means of refined neurological examination and precise rational reasoning.

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C.T. van Valkenburg *1872-1962* 27

R. P. M. Bruyn and G.W. Bruyn

In a certain sense the demise of the nonagenarian van Valkenburg marked the end of an epoch in the neurological past of the Netherlands. He was a contemporary of those other Dutch neuro- dinosaurs like Winkler, Brouwer and Ariëns Kappers. Yet, his death went almost unnoticed, scarcely causing a ripple in the quiet waters of the neurological landscape. Of course, he had outlived most of those who knew him sufficiently well to organise a commemorative event. He, in turn, was outlived by those who did not know him well enough, and could (or would) not. His seclusive lifestyle in advanced years, his ultimate painful illness, and possibly his 'difficult' personality might explain the silence, but there might also have been other, latent, factors at play. Brouwer devoted some words to him on the occasion of van Valkenburg's 65th birthday and his 40th anniversary as a physician, as did Biemond (and the psychiatrist Rümke) when he reached the age of 80. The psychiatrist van der Horst wrote an eloquent obituary, but the leading neurologists at the time remained taciturn.

Highly talented, unswervingly carrying out his duties as a physician, courting an eventually spartan way of life, taking short holidays with his third wife in the Dutch countryside in advanced age, erudite van Valkenburg constitutes a tragic figure. The following pages should be, though somewhat belated, a tribute to this singular man.

Christaan Theodoor van Valkenburg was born in Winschoten, 9 December 1872 as one of six children of a family figuring in the 'blue-book' series (see *Nederlands Patriciaat*). Following the usual primary and secondary school (Gymnasium) education, he enrolled in the Medical Faculty of the University of Groningen in September 1891 and qualified as a physician in 1897. Soon after, he successfully passed his doctoral thesis *On the origin of the fat in fat-embolism*, prepared under the mentorship of Prof. R.A. Reddingius (May 27, 1898).

Figure 1. Christaan Theodoor van Valkenburg in 1898 (marriage).

He settled in Dieren, a village about 10 km northeast of Arnhem, to practise general medicine, which, at the time, included quite a bit of minor surgery as well as obstetrics. He was absorbed by his work; nothing apparently indicated that he was not going to remain a general practitioner for the rest of his life.

For obscure reasons, the unknown young country doctor must either have felt progressively dissatisfied with his work or he developed a growing interest in nervous system diseases (or maybe even both). He succeeded in obtaining the position of assistant in the laboratory of von Monakow in Zürich. One might suppose that Winkler was instrumental as an intermediary in establishing the 'Zürich –connection' upon van Valkenburg's request, but there is no information available claiming that van Valkenburg knew Winkler any better than he knew von Monakow. Given the documented fact that van Valkenburg wanted to specialise in neurology and psychiatry, and that his mother-in-law paid an amount of DFl. 3.000, - annually (at the time a considerable sum) to defray all necessary expenses for a family abroad, one could well ask why van Valkenburg, thus ensured of financial independence, did not seek a position for specialisation in his home country. The implausibility of the supposition mentioned above is strengthened by a remark van Valkenburg wrote down in a collection of essays many years later (van Loghem et al. 1952): "The greatest figure of the three (Winkler in Amsterdam, Jelgersma in Leiden, and Wiersma in Groningen) was indubitably Winkler, incontestably the père noble of Dutch neurology. He put his stamp on a great many pupils, of whom I may but mention Brouwer in Amsterdam and Stenvers in Utrecht. But those who did not sit at his feet as members of the audience experienced his stimulating influence too. After my return from Switzerland, I, probably more than many, have had much to thank him for."

We put this unsolvable mystery aside. Van Valkenburg together with his young wife and children left Dieren for Zürich in 1904. During the two years of work there, he acquired a thorough and intimate knowledge of neuroanatomy. It was said that he knew by heart the immense collection of specimina in the laboratory's museum and studied the structure of the CNS with the aid of the new staining techniques developed in those years. There, the 32-year old heard the true call of his life. He acknowledged his grateful indebtedness to von Monakow in his first publication (*Neurol. Zbl.* 1906 and, in 1932, in the *Gids*).

On returning to his home country, he obtained the position of psychiatrist in the mental hospital Meerenberg in Santpoort (1906-1909), a position that was difficult to obtain, as it was one of the very few available to married men. In this period, his first publications appeared on topics that occupied his mind for years to come, such as cortical localisation, the organisation of central sensory representation, CNS hodology (corpus callosum), and aphasia.

His career accelerated rapidly. He established a private neuropsychiatric practice in Amsterdam, and accepted the invitation to become deputy-director of the newly created Central Institute for Brain Research headed by Ariëns Kappers. Together, they rendered this Institute a rapidly growing international fame. Once the Institute was well on its way, van Valkenburg changed his position there for the one of Director of the Hospital for Epilepsy in 1913; later, as its Chairman of the Board, he reorganised it thoroughly, and it acquired national repute under its new name, the Alexander van der Leeuw Kliniek (1919). In addition, from 1917 onwards, he started to serve (for well over 40 years) the *Dutch Journal of Medicine* in various functions; ultimately making him uniquely suited to write the *livre centenaire* of that journal (1957). Meanwhile, he had become neuro-psychiatric consultant at the Burgerziekenhuis, and in 1909, joined by a group of men of congenial minds (D.M. van London, K.H. Bouman, J.K.A. Wertheim Salomonson, C. Winkler, L.J.J.Muskens, Ernst de Vries, and C.U. Ariëns Kappers), initiated the creation of the 'Society of Amsterdam Neurologists.' A complete list of the founding fathers of this Society – the voice of which dominated Dutch neurology for many decades – is reproduced in the brochure by Faasse and van Gool (1999). Van Valkenburg was instrumental in the publication of all the lectures held at the meetings of said Society from its inception and wrote the introduction to it (1949).

In addition, van Valkenburg had been admitted as Privaat-Docent at the University of Amsterdam, a position he relinquished in 1916, though he was a gifted teacher. The reasons for this decision are obscure; had he stayed, his career might well have been an academic one. He published an impressive series of 'clinical neuropsychiatric observations' from his experience as a consultant at the Burgerziekenhuis, a thorough study on aphasia, and a monograph on localisation in the CNS (1913). The oldest neurological organisation in the USA (The Neurological Society of Philadelphia) invited him to become an overseas member. Like Brouwer in the Henschen-von Monakow controversy, van Valkenburg came to figure among the actors on the international forum (a role few Dutch neurologists, in contrast with their anatomical colleagues, were favoured to play) in his polemic with Niessl von Mayendorf on the cortical organisation of sensation, in which van Valkenburg attributed a decisive role to the parietal lobe and thalamus in the distinction between perception and feeling.

Despite his meritorious record, his didactic talents, his wide clinical experience, his encyclopaedic grasp of neuropsychiatry, his profound neuroanatomical knowledge, his social involvement, his managerial sophistication, and his ever growing list of professional publications, more than amply qualifying him for the highest academic position, the goddesses of fate had decided otherwise along the lines of Hellenic drama. When Winkler left the Chair in Amsterdam for the one in Utrecht (1916) his advice was that he should be succeeded by either Wertheim Salomonson or van Valkenburg. However, this was overridden by the higher authorities who nominated K.H. Bouman (see chapter 30). When Winkler retired from Utrecht (1925), his advice that van Valkenburg should succeed him met a similar rebuttal in favour of L. Bouman. When Jelgersma retired from the Leiden chair in 1930, Rademaker's repeated and stringent advice to shortlist van Valkenburg as the first of three nominees encountered some curious juggling of names, with Carp ultimately being appointed. Shortly after this, the Swiss University authorities refused to heed Winkler's advice to nominate van Valkenburg as successor of von Monakow and appointed Minkowski instead. Such an incredible series of disappointments (*ad verbum facta*) would have broken the spirit of a lesser man.

Steadfast van Valkenburg, however, continued to fulfil the physician's duty. He was nominated honorary member of the Society of Amsterdam Neurologists on the occasion of his 65^{th} birthday and his 40^{th} anniversary as a physician in 1938. He received the distinction of 'Commander in the House-Order of Oranje'" for his successful clinical treatment of Prince Bernhard, the Prince Consort, who had sustained a serious road accident in his cabriolet (1936/1937). Royal friendship was bestowed upon him: his grandson, Prof. Dr J. Bruijn, still has a photograph of van Valkenburg with the royal couple's first baby, Princess Beatrix, which was taken by Prince Bernhard himself in February 1938, in his arms. The photograph of a white-frocked van Valkenburg, as published in the *Dutch Journal of Medicine* in 1938, was also taken by the Prince. Van Valkenburg composed a biography of his close friend, the historian Johan Huizinga, whose study *Herfsttij der Middeleeuwen* [Waning of the Middle Ages] had met international acclaim. Huizinga and van Valkenburg had been class mates and become close friends at the Gymnasium. While pupils there, they had organised the first van Gogh exhibition in that city. When they enrolled at university at the same time, van Valkenburg, Huizinga, and (the famous astronomer-to-be) Willem de Sitter consolidated bonds of friendship as 'year club–mates'.

The firm friendship of the trio, all of whom were fascinated by nature and art, lasted a lifetime, a fact to which several *passus* of van der Lem's biography testify. During their student years, van Valkenburg's youngest sister Dina (later spouse of the Dutch composer Johan Wagenaar) regularly sang songs by Grieg or Brahms in her natural mezzo-soprano voice at their parties, even if de Sitter could have been diagnosed as suffering from congenital amusia, a forgivable defect for someone who was to be the *auctor intellectualis* of the theory of the permanently expanding universe, which at the moment of writing seems to be the most plausible cosmology. Further, Huizinga and van Valkenburg alternated as official witnesses at each other's weddings, Huizinga stayed at van Valkenburg's residence in Dieren once or twice, and van Valkenburg visited de Sitter in Arosa when the latter worked on his theory.

Huizinga, an extraordinarily gifted draughtsman, sketched elaborate graduation drawings for his friends when they passed their doctorate thesis exam; of the few drawings that survived, one depicts van Valkenburg with his right hand holding a stethoscope to a patient's chest, the left leafing through a book, the amphitheater crammed with on-looking patients, the blackboard stating: 'Dr van Valkenburg, consultations 8 a.m.-8 p.m.', and the whole thing framed by two mottoes, one from the mediaeval Bernard de Clairvaux ("Aliquid amplius invenie in sylvis quam in libris" – you will find more in the woods than in the books...) and the other, as well-known as proudly arrogant, from the late mediaeval surgeon Paracelsus (*Alterius non sit qui suus esse potest* – if you can be yourself, do not simulate to be another...). Huizinga later gave his drawings illustrating Dutch history to van Valkenburg who saw to their publication in 1950 and also wrote a biography of his friend (1946). Finally, together with G.G.J. Rademaker (see chapter 25), van Valkenburg wrote urgent medical certificates to the German occupational authorities to release Huizinga from the concentration camp St. Michielsgestel, where Huizinga, together with eight other Leiden professors had been interned as hostages. Huizinga at the time suffered from severe impairment of gait and of equilibrium.

Figure 2. C.T. van Valkenburg in 1961.

Well in his seventies, he was asked to serve as Curator of the Municipal University and to guide the 'purification' procedure in the post-war year 1945/6. This procedure aimed to 'clean' the university's teaching and administrative staffs as well as students of those who, during the German occupation, had shown themselves either to be 'pro-German' or insufficiently 'anti-German' or too lenient, indulgent, or accommodating at decisive moments of time. As chairman of the 'restoration committee', van Valkenburg discharged his duties with fairness, lucidity and wisdom. Some, however, suspected him of not being an impartial chairman, because he had been imprisoned by the Germans temporarily, had given clandestine tuition to students after the Germans had closed the university, and had made his house on the Keizersgracht 728 a despatch address for the underground resistance group of Veeneklaas. In the case of Brouwer (see chapter 19), van Valkenburg's committee advised the authorities the disciplinary measure of a mere "one-month suspension from professional duties." The Minister of Education, however, sacked Brouwer in 1946. Leading Dutch neurologists, in particular Biemond, considered this governmental punishment absurdly incommensurate with the few and slight errors of judgment that Brouwer had committed *bona fides* during his two-year function as Rector Magnificus under the German boot. It was quite right and they saw to it that, as an *amende honorable*, Brouwer was appointed Director of the Central Brain Institute in 1947. Van Valkenburg, who clearly missed the instinct of the typical political animal to avoid situations and positions in which one might make enemies thereby obviating potentially profitable future deals, was suspected to have been instrumental in the ministerial decision. Accordingly his popularity among colleagues was not enhanced. If he was subsequently shunned by his colleagues, one is again tempted to recognise the Hellenic drama-theme of the 'guilty innocent'. A laudation on the occasion of van Valkenburg's 80th birthday was written by a psychiatrist, Prof. H.C. Rümke (1963), and another psychiatrist, Prof. L. van der Horst, wrote a laudation as well as an extensive obituary on the occasion of van Valkenburg's 90th birthday and death, respectively. Furthermore, no Festschrifts nor special issues of the home-journal appeared dedicated to van Valkenburg's 80th or 90th birthday nor to his 50th or 60th anniversary as a physician.

To some extent, his personality may have predestined him to a *carrière manquée*. He was what is usually described as a 'difficult' character, with an extraordinary capacity for admiration as well as for scorn fed by strong emotions that were mostly kept in rein by self-discipline and sharp intelligence. Because of his temperament, his fierce sympathies and antipathies, and his polite but mercilessly sharp tongue in debate, his enemies exceeded his close friends in number. His colleagues feared him during scientific meetings because of his rather critical comments, which antagonised them as needlessly as unintentionally. Averse to extravagance and waste, he was inclined to court a sober and frugal lifestyle, which colleagues jokingly referred to as tightfistedness. His style of speech and writ betrayed linguistic mastery, succinctness, and unequivocality, and displayed transparence. Though he unselfishly gave more than ample time to students in discussions, his level of teaching remained profitable for the gifted few only. Accordingly, he had no 'pupils'; probably because of the brief and quick thrusts of his sword-like tongue they all died *la mort sans phrase*.

Apart from commanding an exceptional grasp of the neuroanatomical, neurological and psychiatric literature of his time, van Valkenburg was a cultural erudite, a typical elitist, abhorring *hoi barbaroi*, intimately familiar with European painting and *belles lettres*, lover and collector of (classic) art, fond of surrounding himself with antiques collected during the frequent voyages to Italy with his first wife, mostly reading works on history, prone to philosophise, progressively engrossed in a world of ethical and aesthetical refinement: the Apollinic came to fully prevail over the Dionysian component of his existence.

In addition to the above-mentioned personality traits, the fact that he was a firm atheist is quite likely to have played a major role in his unfortunate academic career, if one recalls the prevalent Calvinistic atmosphere of Dutch Academia at the time.

Up to one year before his death, van Valkenburg remained scriptorially active, as is to be expectedof a workaholic. The terms hobby and leisure activities shone by their absence in his vocabulary. He knew only one 'hobby': his profession. His list of publications includes some 150 items, a small selection of which was published by van der Horst (1963). None of them are referred to any more. Yet, this sketch of a unique Amsterdam neurologist would be incomplete without a brief outline of his chief professional topics of interest. These included the central organisation of extero- and interoception and the epistemological problem of the localisability of nervous functions, the last-named bearing on aphasia in particular. These chief topics caught his fascination after an early series of studies on parieto-occipital hodology, the corpus callosum, the mammillary bodies, the cerebellar cortex, and the trigeminal root system. In the course of a wide range of publications on clinical neuropsychiatric problems, he described an intriguing symptom of cerebral concussion, namely post-concussional lymphopenia (1933). Checking for this symptom fell into practical disuse and oblivion, though, in the 1950s, it was still regularly looked for in the Utrecht Department of Neurology. It later turned out to be a non-specific component of Selye's acute stress syndrome.

With respect to the localisability of nervous functions, van Valkenburg maintained a reserved attitude. During the years of his formal medical and anatomical training, the optic semi-decussation had only recently been established and the retinal- striate cortex projection controversy settled. The localisation 'fanatics' such as Broca, Flourens, Liepmann, Wernicke and Lichtheim went too far in his opinion. His teachers, von Monakow, Pierre Marie and Hughlings Jackson, were completely against the localisation dogma of functions. At the root of this controversy was von Monakow's diaschisis concept. Van Valkenburg emphasised that the truth lay in between. He argued that loss of function after a lesion does not permit one to localise that particular function exclusively to the site of that lesion without further qualification, because a) the interconnectivity within the nervous system is so astronomical that it is impossible to obtain all the necessary , and b) an identical loss of function could well be produced by a lesion elsewhere. The site of a certain lesion can inhibit other sites or circuits that are more essential to the maintenance of the lost function, or are only facilitatory, or cause the release of inhibitory control sites. This would apply in particular to aphasia, and one has only to recall that in diaschizis, the paralysis is initially flaccid but becomes spastic later on without any change to the site of the lesion. One can, indeed one must, localise a lesion, but one cannot hope to localise a function, a faculty, precisely.

As to sensation, he considered that sensory afferences play the key role in the quintessential function of the cortex, which is the adaptation of nervous actions and reactions to experience. The primary afferent has a 'local' element only by virtue of the level (and extent) of structural organisation of its arrival site, as well as the preceding organisation of the intermediate thalamic relay. (The reader may realise that in this concept, vague as it may sound, van Valkenburg anticipated the Penfield homunculus as well as the homunculi of the thalamic VPL and VPM nuclei. The discovery that, for example, the cortical representation-area of the thumb, mouth and forefinger substantially exceeds that of the leg, and that the strength of the stimulus arriving in such a representing area determines the extent of it, was made only a few decades ago.) The primary local afference in the posterior central gyrus may exert immediate effect in the anterior ventral gyrus organisation of motoricity, but has a 'double' representation in that it also becomes a component of the parietal cortical network, which renders the primary afference the information of position within the 'sensation–space', whether interior (body-schema) or exterior. Moreover, synchronous optic, vestibular, and cerebellar input are a *conditio sine qua non* in this process. When the arriving 'local-value' stimulus becomes embedded in the parietal circuitry, the local feature and its objective signal quality acquire the quality of a 'feeling' rather than of a mere 'perception'. Van Valkenburg pointed out that the 'double' representation is anatomically founded in the observation that the cortico-cortical afferents from the corpus callosum terminate in cortical layers V and VI, to link-up homologous and non-homologous fields of the right and left hemispheres, whereas the thalamocortical afferents would terminate in other layers (1913). He advanced this concept half a century before Szentagothai proved the columnar organisation of the cortex and adduced a detailed map of the various categories of sensory cortical input, which, though thoroughly modifying van Valkenburg's thesis, left it basically intact.

Van Valkenburg's proposal, made on the basis of a study of 'higher order paraesthesias' and pain, namely that central autonomic (vegetative) dysfunction is decisive for such clinical phenomena as the 'lost hand or limb', kinaesthesias (and one may add coenaesthesias), as well as for the mental involvement that make the mere perception of pain a bothering experience (1937), has not been subject of further study. Furthermore, as far as we are aware, there have been no studies devoted to his idea on the role of autonomous nervous system activity in derangements of the body scheme.

Even in the last year of his life, when he suffered from an ultimately fatal aorta-aneurysm, he spent his holiday in the countryside. The long walks he usually took with his wife were now beyond his capability. On Friday December 7, 1962, the laudatory text that L. van der Horst had written on the occasion of van Valkenburg's 90th birthday was published in the *Dutch Journal of Medicine*. Van Valkenburg's wife read the text to him, which, according to a subsequent statement by the journal's editors, gave the patient some moments of contentment, consolation and relief. He died the next day. With him, the last Dutch citizen of the neurological Parnassus disappeared.

He was interred in the cemetary 'Zorgvlied' in Amsterdam. His grave has since disappeared too.

The only thing that officially reminds the medical body of our country of a unique neurological colleague is a portrait of him, drawn by the prominent artist Jan Sluijters, which hangs on the wall of the conference room of the Society of the *Dutch Journal of Medicine* in Amsterdam.

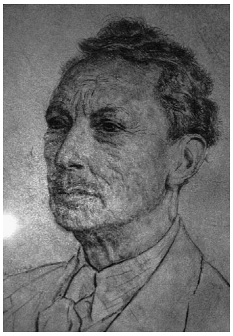

Figure 3. Drawing of C.T. van Valkenburg bij Jan Sluijters in 1946.

There is almost nothing about his private or family life to be gleaned from the available documentation. Even in an essay that was meant to be personal, he carefully avoided statements about himself (van Loghem et al. 1952). A search of the archives of all the daily papers in the Koninklijke Bibliotheek and a search of the archives of the NRC/Handelsblad by Mrs. S. Looijen yielded a single notice of van Valkenburg's death in the conservative- liberal evening newspaper NRC/Handelsblad of Monday, December 11, 1962. The notice runs as follows: "On Saturday 8th December our stepfather, C.T. van Valkenburg, passed away. Signed: L.Ph. LeCosquino de Bussy. A.E. LeCosquino de Bussy-de Lange." As it is customary in the Netherlands for surviving next of kin to put fairly detailed announcements of death of a close relative in the daily journals, this short and single notice seems curious. Subsequent personal communication with the single surviving stepdaughter (Mrs. A.E. de Bussy-de Lange) as well as with the surviving grandson (Prof. Emer. Dr J. Bruijn, Prof. of History of Art) clarified at least part of the enigmatic and unknown background of van Valkenburg. His character bore the typical features of a 'Groninger': rather reticent, unaccommodating, stubborn, and guarded. He was a rather forbidding, lean person, but one who was able to show great warmth and unflagging loyalty, once you had won his sympathy. Shortly after passing his thesis, he married Wilhelmina Adriana van Roijen, daughter of a locally well-known and wealthy Groninger family, the fortune of which was of colonial origin and the history of which can be found in a monograph authored by a grandson Mr. W. van Heuven. The marriage was blessed with the births of two daughters, but ended in divorce after 33 years (October 1931); Wilhelmina Adriana died in 1937. He married a second time to a divorcee, Mrs Marie Henriette LeCosquino de Bussy-Vis, in Poole near Bournemouth (England) in July 1932; she died in May 1956. The same year, in September, at the age of 80, he married Ms Christina Roos, whom he had known for decades as the matron at the Burgerziekenhuis and who took extremely good care of him in the final years of his life; she survived him for nearly 40 years, dying at the age of 96 in January 2000.

In the face of this evidence, a biographer can only infer that van Valkenburg could not bear to be without a female partner or companion for extended periods of time , a living paraphrase of the closing strophe of Goethe's Faust: "Das Ewig-Weibliche zieht uns hinan." This agrees with what we alluded to (*vide supra*) as the conflict between the Dionysian and Apollinic forces in his soul. As such, his life's history appears to epitomise the typical rift between Pathos and Ratio, between the Promethean and Epimethean, to which the mind of the strictly brought-up male of the upper-middle class, *nolens volens*, is subject. To stay with Goethe: "Zwei Seelen wohnen, ach, in meiner Brust; die Eine will sich von der Andern trennen; die Eine hält in derber Liebeslust sich an die Welt mit klammernden Organen, die Andere hebt gewaltsam sich vom Dust, zu den Gefilden hoher Ahnen." Van Valkenburg was a living Dr. Faustus figure.

Arguably, academic frustrations, accumulating between the 1920s and 1930s, are most likely to have gradually eroded his capacity to tolerate this internal tension, and, culminating in not being chosen to succeed von Monakow in Zürich (the very place where he and his wife, as he wrote to von Monakow in September 1906, had spent the happiest years of their lives), precipitated the ultimate failure of the marriage with his first love. His first daughter, Elisabeth Bruyn - van Valkenburg died about nine months before her father; his second daughter, Cornelie van Heuven- van Valkenburg died in 1984.

The present authors have had to refrain from including in this chapter an analysis of the large collection of personal letters, which van Valkenburg wrote to von Monakow, his spiritual father, because of the space allotted for this chapter. The collection merits a separate neurohistorical study.

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N.B. Other major papers by van Valkenburg are listed in the obituary by van der Horst (1963).

W.J.C. Verhaart *1889-1983* 28

J. Voogd and E. Marani

Willem Cornelis Jozef Verhaart was born in Amersfoort on August 31, 1898, as the son of an army officer. He received his primary and secondary education in 's-Hertogenbosch. He does not seem to have been an outstanding pupil; at high school (Hogere Burger School) he had to repeat a year. The family moved to Utrecht, where he studied medicine from 1915 till his graduation in 1922. During his medical studies he continued to live with his parents. He was a member of the Utrecht Students Corps, but did not feel comfortable in this ambiance; he never liked drinking alcohol. He specialised in nervous and mental diseases with professor C. Winkler, who occupied the first chair of Neurology in Utrecht and who acted as promotor for his M.D. thesis on *Clinical and Anatomical Investigations of Alzheime'rs disease* (Utrecht, 1925). Verhaart always considered H.W. Stenvers (see chapter 26) as his true mentor in clinical neurology. He met his future wife, Johanna Anna Bolderij (St. Anna ter Muiden, 1899 - Leiden, 1978) during their medical studies in Utrecht. They married in 1925 and had one son, Pieter (1929). After the completion of his residency, Verhaart was employed as a house doctor at two psychiatric hospitals. First at the Provincial Hospital in Medemblik (J.G. Dikshoorn) from 1925 till 1927, and then until 1930 at Oud Rozenburg in The Hague (H.A. Gerritsen), where he installed his first anatomical and neuropathological laboratory.

In 1930, the family moved to Batavia in the Dutch East Indies, where professor P.M. van Wulffen-Palthe had offered him a position as assistant in the department of Neurology and Psychiatry of the Batavia Medical School. In 1932, he started his lectures as a private instructor at the Medical School with a public address 'About the development of the central nervous system of vertebrates and its significance for the histopathology and the clinics of nervous diseases.' During these years Verhaart and his wife both ran a private practice in Batavia.

In 1938, Verhaart worked at the laboratory of Fulton and Dusser de Barenne at Yale University, Connecticut, U.S.A., as a Rockefeller Foundation fellow. There, he collaborated with Margaret A. Kennard on the connections of motor and suppressor areas of the cerebral cortex of the monkey (Verhaart and Kennard 1940). Some of the correspondence that took place between Verhaart and Fulton between 1937 and 1959 is cited in a paper by Koehler (in press), which concerns the correspondence between Bernard Brouwer and John Fulton in the same period.

Shortly before the outbreak of the war with Japan in 1941, Verhaart enlisted as a medical officer and was detached as neurologist at the military hospital in Tjimahi. He was interned as a prisoner of war, first in Tjideng and Tjimahi, later, separated from his family, in Batavia, and in the Green Valley Camp in Singapore. In 1944, he was transported to Pakanbaru in Sumatra, where he acted as a doctor for the Dutch, Australian and British prisoners of war who suffered from hunger and tropical diseases during their forced labour in the building of a regional railway. His first letter to his wife, after the capitulation of Japan, mentions his camp experiences in staccato style, the support of his buddy, the dermatologist Robbie (D.G.P.H. Simons), the concerns about his son ("Will he still recognise me? Will we get along? Will he know everything better than me? I am hoping for the best!"), and ends "the only things I have learned during this period is smoking a pipe and hanging around, but that will pass away again." In 1945 he was reunited with his family in Batavia. His wife Jo had served as a doctor-in-chief in the internment camps for women and children of Tjideng and Kramat. After a reconvalence of the family in Melbourne, Jo travelled to her mother in Holland as a ship's surgeon on the M.S. Sibajak, and returned on the M.S. Oranje, to take up a position as director of the Tjikini Hospital, while Verhaart resumed his duties, first as a lecturer (1945), later as a professor in Neurology and Psychiatry (1946) at the Medical School of the University of Indonesia in Batavia, known since 1946 as Jakarta.

They returned to Holland in 1952, where Verhaart spent some time as chief assistant to professor G. Rademaker, the director of the department of Neurology of Leiden University (see chapter 25), as neuropathologist at the Psychiatric Hospital Endegeest, in Oegstgeest (J. Stotijn), and as a guest of professor J. Dankmeijer at the Anatomical-Embryological Laboratory in Leiden. In 1953, he was appointed to the chair of Histology and Microscopical Anatomy in Leiden, as the successor of professor S.T. Bok. His inaugural address on May 29 carried the title 'Stimulus-pattern and fibre-pattern in the nervous system'. There he founded a neuroanatomical laboratory, which he developed into a centre of international repute. As professor and director of the newly founded Institute of Neurological Sciences he also supervised, from 1958 on, the clinical departments of Neurology (W. Kramer) and Neurosurgery (prof. W. Luyendijk). He retired in 1968, reading his farewell address on January 24, 1969 in the Laboratory of Anatomy and Embryology, where he had worked for almost 20 years. A special issue of *Psychiatria, Neurologia, Neurochirurgia* (Luyendijk et al. 1969) was published on this occasion, and his portrait was painted by H.H. Kamerlingh Onnes (at present hanging in the Department of Physiology in Leiden).

During his active years in Leiden he was assisted by a loyal administrative and technical staff: the secretaries Miss To van Goor and Miss Irma Saveur; his long-term support, before and after his retirement, Mrs. W. Parmentier; Mr. Wim Meyers, who processed the six photographic plates he took every morning at 8.00 o'clock sharp; Mr. Rovers, who took care of the cats and monkeys, the blind capybaras, the tupaias, goats, bats and parakeets of his varied, experimental menagerie; and Els Kükler, the formidable cleaning lady. Professor Verhaart died on May 26 1983 in Leiden, aged, and lonely, as his wife had died from Alzheimer's disease in 1978, following a long illness. An *in memoriam* of Verhaart appeared in the *Nederlands Tijdschrift voor Geneeskunde* (Voogd 1983).

His attitude as a scientist is, perhaps, best characterised by the peroration of his inaugural address in Leiden, directed at his students. "A scientific investigation often seems endless, although it appears to be completed quite often. While working, you often feel that you started off from the wrong premises, but this is only a sign of growing maturity. The research seems to go astray, but that just means that you have followed new, untrodden paths. Results are often lacking, but that is the consequence of your growing powers of discrimination, and the oblivion of your original assumptions. Research seems monotonous and tedious, but it is less so than any other kind of occupation. Between the moment of an eager start and a satisfactory ending, despair is a natural and innocent phenomenon. When you are prepared to endure these inconveniences, I will be glad to assist you."

Verhaart authored 175 publications (Luyendijk et al. 1969) and supervised 22 doctoral theses; the first two by W. Kramer and Geertruida A. van Wieringen-Rauws were defended in Djakarta, the others in Leiden. In 1969, when the Norwegian anatomist and resistance hero, professor J. Jansen, received an honorary degree from Leiden University, Verhaart acted as his promotor. Verhaart's papers are mostly descriptive, and illustrated with photographs. He was an excellent photographer, who documented his observations in thousands of prints, with his scribbled annotations in the margin, which are still kept at the Department of Physiology in Leiden, and whose life and travels can be followed in his family pictures. He could not draw and distrusted diagrams, "which, as all simplifications, do not match reality" (Verhaart 1932) "and often remind one of diagrams of the human body, like those of the Earth from the Middle Ages which were not only wrong, but also obstructed science" (Verhaart 1968).

Together with professor Dankmeyer, and others, he founded the 'Neuroanatomical Study Group' in 1952, a national forum, where students from the Brain Institute in Amsterdam, the Departments of Anatomy in Rotterdam, the Vrije Universiteit in Amsterdam, and the Department of Zoology in Leiden, neuropathologists from the Ursula Clinics and other neighbouring institutes (J. Tans, V.W.D. Schenk, W. Kramer, H.C. Jelgersma), and guests from all over the country and from abroad, met to present and discuss their work. Before his retirement in 1968, the group had held almost 100 monthly meetings, where 250 papers were read. Verhaart was probably the only member to have attended them all. The meetings were continued under his name until 1993. Verhaart's pronouncement, during one of the meetings, that "we are only interested in fibres, not in cells," exasperated some of his guests, but was rather typical of his idiosyncratic approach of neuroanatomy.

Verhaart was an avid reader. During his lunch break he often read about history. In the evenings and weekends he read through a score of neurological and anatomical journals. It was a rare occurrence to be able to show him, at one of the three weekly journal clubs he attended, a paper that had escaped his attention. He usually came up with an abstract of the paper, excerpts which he always typed on an old typewriter, on scraps of low-quality paper. Verhaart was a frequent visitor of the Society of Amsterdam Neurologists, where one would invariably find him in the first row of seats, among his esteemed colleagues, Biemond, Grewel, van der Horst and Stenvers, all of whom died before him. He was appointed an Honorary Member of the Society in 1980. Verhaart was an active member of the Neurosurgical Study Club. He often lectured, on some new aspect of the comparative anatomy of the brain, at the meetings of the Dutch Association of Anatomists. During some of the non-neurological presentations at the autumn meeting of the Association in Amsterdam, he used to take us to the zoo at Artis, to contemplate the brains *in-situ*. Together with J. Droogleever-Fortuyn and H.G.J.M. Kuypers, he edited ten volumes of the series *Studies in Neuroanatomy*, which included a number of theses and two of Verhaart's monographs. Verhaart's students became neurologists, psychiatrists, neurosurgeons, general practitioners, pathologists, zoologists and anatomists. Quite a few of them subsequently occupied chairs or lectureships: in neurology in Leiden (W. Kramer), Rotterdam (A. Staal, H.F.M. Busch, H. van Crevel), the Universities of Amsterdam (H. van Crevel), Jakarta (Sie Pek Giok, Priguna Sidharta) and Kaapstad (A.S. de Graaf); in neurosurgery (Leiden, W. Luyendijk); in electrophysiology (K. Mechelse, Leiden, Rotterdam); in pathology (Rotterdam, N.J.A. Noorduyn); in zoology (Leiden, J. Dubbeldam); in anatomy (Free University of Brussels, Leiden, Rotterdam, J. Voogd); and in neurophysiology (Sofia and Stara Zagora in Bulgaria, Technical University of Enschede, E. Marani).

Verhaart changed the face of neuroanatomy by the introduction of the Häggqvist method, a modification of the Mann-Alzheimer methylblue-eosin stain, which allowed one to visualise individual myelinated fibres in the central nervous system, and made it possible to study the fibre-pattern, the visual impression of the heterogeneity in fibre-calibre of nerve tracts, and the fibre-spectrum, i.e., the quantification of this heterogeneity. The contributions of Verhaart and his students have been recently reviewed, and put into a more general perspective, by R. Nieuwenhuys (1998). Verhaart initiated and continued studies of the anatomy of the human brain and spinal cord, together with Sie Pek Giok, Th.B. Gebbink, D.J. Lankamp and J.R.H. Schoen. Results were published in the theses of the former three students; Schoen died in 1981, before he had completed his thesis. Some of his data were published in a posthumous review (Voogd et al. 1990) and in a monograph on the trigeminal system (Usunoff et al. 1997). To assure a continuous stream of human material, Verhaart took charge of neuropathology at the Central Laboratory of Pathology in Rotterdam (M. Straub, J.A.J. Spaas, F.C. Kuipers and C.B.F. Daamen), the pathological laboratory of the Zuidwal Hospital in The Hague (P.M. Bakker), and the Leiden Department of Pathology. His skill with Meynert's dissection of the brain, by which the brain stem, together with the basal ganglia and the insula, is separated from the rest of the hemisphere, amazed and, sometimes, dismayed bystanders. This trick, and his running commentary, mainly served to hide his greed for intact brains to take back to the lab for his anatomical studies. It also gave him the opportunity to pursue his long-standing interest in neuropathology, such as his studies on encephalopathy in children, which date from his collaboration with the pediatrician prof. J.H. de Haas in Batavia (Verhaart 1932a, 1971).

Verhaart was the first to identify the efferents of the striatum as numerous thin, poorly myelinated fibres, and to distinguish them as well as their targets, from the heavily myelinated fibres of the globus pallidus (Verhaart 1950, 1957). His early studies on the pathology and the variability of the cerebral peduncle and the pyramid awakened his interest in experimental and comparative neuroanatomy (Verhaart 1931, 1932b, 1935, 1947, 1967). When observing the survival, after extensive cortical ablations, of the numerically substantial contingent of small fibres in the pyramidal tract, he was at a loss to explain their origin (Verhaart 1947). This enigma was solved in collaboration with van Crevel, who discovered the different, exponential degeneration rates of large and small fibres in the pyramidal tract, and used this information to calculate the contributions of different cortical areas to this tract (van Crevel and Verhaart 1963a,b). His *Stereotactic Atlas of the Brain Stem of the Cat* (together with G.T. van Beusekom, H.F.M. Busch, A. Staal and J. Voogd 1964) is based upon the theses of his co-authors, and illustrates the beauty and the power of the Häggqvist method.

Early on, Verhaart's interest was caught by the variability among species of the red nucleus and its efferent tracts, the rubrobulbar and rubrospinal pathway and the central tegmental tract (Verhaart 1936). In later publications he made important contributions to the definition of these pathways, and to their origin and termination (Verhaart 1955,1956, 1957b). In 1962, he showed the dependency of the occurrence of olivary hypertrophy from the integrity of the cerebellum, rather than from a lesion of the central tegmental tract, in a study using the brains of cats, originally operated on by Rademaker, and left in the attic of the department of neurology for several decades (Verhaart and Voogd 1962). His comparative neuronatomical studies started with Mary-Rose Soper-Jurgens' (re-) discovery of two massive tracts in the mesencephalon of ungulates, the trigemino-thalamic tract of Wallenberg and the bundle of Bagley, which detaches from the cerebral peduncle at a high mesencephalic level (Verhaart and Sopers-Jurgens 1957). Goats were used in the experimental verification of the origin of these tracts (Verhaart and Noorduyn 1961, Verhaart and Haartsen 1967), and served the dual purpose of providing the lab with *sateh kambing*. Foreign guests contributed to the diversity of the research, like David Bowsher (Department of Anatomy, Liverpool, U.K.), who studied the anatomy of sensibility (Bowsher 1965), Azarias Karamanlidis (Department of Veterinary Anatomy, Thessaloniki, Greece), who started his experimental studies on the goat trigeminal system in Leiden (Karamanlidis and Voogd 1970), and Irena Grofova (Department of Anatomy, Prague, Czechoslovakia), who traced the entopeduncular-subthalamic pathway in a bear, which Karamanlidis had bought from a local gypsy (Grofova 1970). Verhaart's two volumes on *Comparative Anatomical Aspects of the Mammalian Brain Stem and the Cord* (1970) are lasting proof of his careful observation and his wide-ranging interest in the comparative anatomy of the brain. Much of the material used in his comparative studies was provided by P. Zwart, pathologist of the Department of special animals at the School of Veterinary Medicine in Utrecht, and from the collections of the Netherlands Institute of Brain Research in Amsterdam, through the good offices of the comparative anatomist professor Rudolf Nieuwenhuys. Verhaart's own slide collection, counting approximately 10.000 specimens, including a number of primate brains he brought back with him from Indonesia, is kept at the Department of Physiology in Leiden. Verhaart's last paper concerned tracts in the brain stem of the parakeet, a subject he inherited from his former student, A. Zecha, which he studied after his retirement, in a back room in the basement of his former department (Verhaart 1976).

Verhaart published extensively on clinical neurology, especially during his years in Indonesia. In the *Psychiatrische en Neurologische Bladen* alone, he published 15 clinical papers between 1925 and 1958, on such varied subjects as Alzheimer's disease, the pathophysiology of the 'paraplégie en flexion', anencephaly and other inborn errors, demyelinating diseases, encephalitis and the neurological complications of malaria. He described what are among the first cases of 'multiple system atrophy' or "heterogenous systematic degeneration of the central nervous system," as Verhaart called it (Verhaart 1940, 1958). His lecture notes on diseases of the basal ganglia bear tribute to his extensive knowledge of this field (Verhaart, unpublished). His clinical acumen, mixed with a taste for absurdities and a vivid interest in the peculiarities of his peers, resulted in an endless stream of observations and anecdotes, communicated to us during coffee time. At these memorable daily occasions, the most recent graduate had to vacate his chair, next to the professor, to the following candidate, who anxiously awaited Verhaart's admonishing remarks, supplemented with the tapping with his signet ring on the table, and the extensive, scribbled annotations on the chapter he had submitted the day before.

Verhaart was modest and sober, with a rigid time-schedule, in his Leiden years mainly devoted to reading, writing and microscopy. He did not like empty social conventions, but liked to share opinions and experiences with his students and their spouses, his friends and colleagues. During his retirement the 'small' walking club with professor S E. de Jongh, professor D. Wiersma and others, also served this purpose.

His greatest scientific contributions, probably, are in the field of the microscopical topography of the central nervous system, where he introduced the concept of the fibre pattern, to characterise, delimit and quantify fibre systems, as a basis for experimental tracing of fibre pathways and to study their variability within and among species. With his self-criticism and scepticism, he was not inclined to parade his achievements. His ideas can be traced in the scientific careers of his students, whom he allowed complete freedom in their research and who remember him with great affection.

Figure 1. Verhaart at 4 years, with his sister.
Figure 2. The young clinician, 1923.
Figure 3. Verhaart and his wife in her office in the Tjikini hospital, shortly after the war.
Figure 4. With Jan Jansen at the occasion of his honorary degree in 1969.
Figure 5. Self-portrait, 1970.
Figure 6. With Mrs. Verhaart-Bodderij at his farewell lecture in 1969.
Figure 7. Verhaart, 1968.

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J.K.A. Wertheim Salomonson 29
1864-1922

R.P.M. Bruyn

Figure 1. J.K.A. Wertheim Salomonson.

Perhaps only a handful of practicing Dutch neurologists today are familiar with the name of a man, who was deeply involved in the birth of neurology in the Netherlands. This might be due to his penchant for biophysics (although he was quite active in clinical neurology) as well as to his modesty and reticence, or to his inclination to pursue physical problems, to tinker in his laboratory, and, as a pioneer, to develop roentgenology into a clinically useful tool. Be that as it may, not much is known about his private life, personal idiosyncracies, friends, cultural preferences (music? literature? travel?). Therefore, the appearance of the present book offers an appropriate opportunity to honour the memory of one of the great Dutch pioneers in neurology and roentgenology.

Johannes Karel August Wertheim Salomonson was born on February 18, 1864 in the small village of Ambt-Almelo, in the eastern part of the Netherlands, near the German border. His father, Maurits Salomonson, married to Sophia Rosette Wertheim, was director of the Royal Steam Spinning Mill at Nijverdal at the time the Dutch textile industry flourished in the province of Overijssel, i.e., the eastern part of the country. For obscure reasons, Maurits Salomonson was granted by the Royal decree of April 24, 1860, no. 73, the right to add the name Wertheim to his own (Luyendijk-Elshout 1984). Possibly, Maurits's request was motivated by the absence of male descendants in the Wertheim family, and, therefore, by the aim to prevent the name 'Wertheim' from extinction. Johannes' mother wrote poetry under the pseudonym 'Madeleine'. He married Henriette Johanna Estella Heymans on December 27, 1894. The marriage remained childless.

He received secondary education at the HBS (Higher Burgher School) in the town of Almelo for the first three years and in the town of Zutphen for the final two years. There, the physics teacher, Goudsmit, exerted major influence on his development. He enrolled in the faculty of medicine at Leiden when he was 17 years old, qualified in 1886 and defended his M.D. thesis *Stereognosis* in 1888, earning the predicate '*cum laude*'. A search in various university archives, the Album Promotorum, and the Catalogus Candidatorum failed to produce the identity of his promotor; possibly this was Professor Samuel Siegmund Rosenstein (1832-1906), the 'patriarch' of internal medicine in the Netherlands, but equally it may have been Professor Einthoven (1860-1927), the physiologist. The thesis betrays his marked talent for mathematics and physics, which subsequently led him to devote his activities to electrodiagnostics.

Leaving Leiden, Wertheim Salomonson became assistant to the Professor of Internal Medicine at the University of Amsterdam, Pieter K. Pel (1852-1919), who had been assistant to S.S. Rosenstein (1832-1906). Following this two-year training in internal medicine, he obtained a physician's position in the 'policlinic for electrotherapy', headed by Dr C.C. Delprat. When Delprat left, the directorate of this clinic was assigned to Wertheim Salomonson, who, inspired by G.B.A. Duchenne de Boulogne (1806-1875) and W.H. Erb (1840-1921), developed electrotherapy as a new domain of science, and succeeded in making neurology a distinct discipline independent from the tutelage of internal medicine. This was a fact of decisive significance, because, at the time (as can be inferred from the repeated concern by F.C. Donders, C. Winkler and J.N. Ramaer) neurology as a distinct discipline was threatened to be crushed between internal medicine on one side and psychiatry on the other.

Wertheim Salomonson progressively focussed his activities on roentgenology (following Röntgen's discovery in 1891), as he immediately perceived its exquisite value for the practice of medicine. He published the first roentgenogram of a hand in the *Dutch Journal of Medicine* (Wertheim Salomonson 1896a). Wertheim Salomonson's significance for the development of roentgenology as a discipline can scarcely be overestimated (van der Goot 1922, Meyers 1922, Brouwer 1923, Voorhoeve, 1923). He started to study electrical induction and transformation experimentally, analysed electric currents in high-voltage generators, current-interruptors, milliamperometers, and the intensity of roentgenrays. He proved to be a master in the development and refinement of methods and techniques of electric phenomena, as is testified by his method to measure the thickness of the glass-wall of a (roentgen)-tube and his construction of an apparatus to measure the penetration-depth of roentgenrays. He initiated the roentgenographic localisation method of a foreign body anywhere in the human organs, and was the first to call attention to the cutaneous damage resulting from frequent or long-lasting radioscopy (Wertheim Salomonson 1896b). In addition, he refined and improved Willem Einthoven's string-galvanometer (earning Einthoven the Nobel prize in 1924) by the two-step procedure of first argentising the quartz string chemically, and second galvanizing it, which produced a string of extremely low resistance (Wertheim Salomonson 1907, Wijers 1996). This enabled clinicians to substantially enhance the clinical value of electrocardiography. In addition, he designed and developed an apparatus to photograph the retinal fundus (Wertheim Salomonson 1919). He introduced medical photography as a diagnostic aid in the Netherlands and remained one of the most active members of the Dutch Society of Amateur Photographers for over 15 years.

Together with Dr Bollaan (secretary), Dr Huet (treasurer) and eight other colleagues, he founded the 'Dutch Society for Electrotherapy and Radiology' during a meeting in the 'Zuid-Hollandsch Koffiehuis' in Rotterdam, on April 14, 1901, and was chosen as its chairman. The society's name was changed into the 'Nederlansche Vereeniging voor Electrologie en Röntgenologie' (Dutch Society for Electrology and Roentgenology) in 1907. Almost without exception, this society had its meetings in his study-room at the polyclinic between 1901 and 1921. Wertheim Salomonson attended all 44 meetings from 1901, was listed as speaker on 40 occasions, presenting a total of 55 papers, many of which dealt with inductors, condensators, and transformators.

A remarkable lecture on foetal electrocardiograms presented at the Royal Academy of Sciences deserves mention (Wertheim Salomonson 1914), an example of his papers that mostly focused on exploring and improving instruments rather than clinical problems.

He remained chairman of the Dutch Society for Electrology and Roentgenology for quite a number of years (1901, 1903, 1904, 1906, 1907, 1916, 1919, 1920) and received honorary membership in 1911, a distinction that had already been extended to him by the French, German and English Roentgenological Societies. He organised and presided the 4th International Congress of Electrology and Roentgenology in Amsterdam (1908). When 'his' Society celebrated its 25th anniversary, he was made a Knight in the Order of the Dutch Lion.

Wertheim Salomonson continued to be the soul and axis of this Society (Panhuysen 1995). Thanks to his inexhaustible energy, respected both nationally and internationally, this workaholic was still at work just two days before his death, experimenting with wireless telegraph apparatus in order to explore the possibility of transmitting electrocardiograms over long distances. An extraordinary expert in this field, he had been invited by the Dutch government to participate in a committee advising on establishing wireless telegraphy between the home country and its colonies.

His academic career was exemplary: appointed to Extraordinarius in Neurology, Electrotherapy and Radiography in 1899, he read the introductory address on January 29, 1900, entitled 'On the Neurone-Doctrine'. On that particular date, he became the first, together with Professor E. Grunmach in Berlin, to assume a university teaching position in roentgenology. As a professor, he became assistant to C. Winkler (who, after his return from the chair of Psychiatry in Utrecht, had become professor of Psychiatry and Neurology in Amsterdam, 1899) and closely collaborated with him from 1900 to 1915.

He was appointed member of the Royal Academy of Sciences in 1912 and, after Winkler had left to assume the professorate in Psychiatry and Neurology at the University of Utrecht in 1915, the municipal council of Amsterdam appointed him as Ordinarius on December 22, 1915, ratified by Royal decree of January 14, 1916. This is where it is necessary to rectify Winkler's statement (Winkler 1930): during the discussion of the Amsterdam municipal council about the appointment, it was not some medical assistants, who objected to Wertheim Salomonson's future Ordinariate because of their doubts about his clinical abilities, rather it was some members of the council (Bellaar Spruyt et al. 1915a,c), who lobbied against the appointment. Instead, 17 medical assistants (Blauwkuip et al. 1915) pleaded by letter to the council in favour of Wertheim Salomonson's ordinariate. His appointment on February 1, 1916, with an annual salary of DFl. 6,000 implied that his rival, C.T. van Valkenburg (see Chaper 27), was left holding the baby. Ultimately, Wertheim Salomonson was called to the office of Rector Magnificus of the University in 1921, a year before his death. Winkler characterised him as a fine, civilised, simple man, of aristocratic mind and eloquent speech, who was widely read, and a witty and crystal-clear writer.

To complete the sketch, Wertheim Salomonson, in conjunction with Winkler, van Londen, van Valkenburg and K.H. Bouman, founded the 'Amsterdamsche neurologische demonstratie vereeniging' (Amsterdam Neurological Demonstration Society) (October 13, 1909), later called the 'Amsterdamsche Neurologen Vereniging' (Society of Amsterdam Neurologists). During its first meeting, on November 8, 1909, he read a paper on the differential diagnosis between hysteric and pyramidal clonus with the aid of the string-galvanometer (Wertheim Salomonson 1909).

His *opera omnia* include 203 publications (Voorhoeve 1923) of which about 85 are of purely clinical slant. At the time, when his well-known colleagues were focusing on neuroanatomical or psychiatric topics, he was an acknowledged expert on peripheral nerve disorders, myositis, nerve tumours, neuralgia and myalgia, to which several chapters to the *Handbook of Nerve Diseases* by Bouman and Brouwer (Wertheim Salomonson 1923) as well as his chapters in Lewandosky's *Handbook* (Wertheim Salomonson 1911) convincingly testify. His clinical eye did not neglect rare disorders, one of which he described as 'tromoparalysis tabioformis cum dementia' (Wertheim Salomonson 1900), a Parkinsonian syndrome associated with abolished tendon reflexes and light-non-responsive pupils, to which, many years later an M.D. thesis was devoted (van der Lugt 1939), but which appears to have gone into oblivion since.

He was a member of the editorial board of *Psychiatrische en Neurologische Bladen* from its inception (1897) up to 1900, and editor-in-chief from 1901 to 1904.

He legated his extensive library to the Royal Academy of Sciences, with the exception of books on medical electricity which he donated to the University Neurological Department. In addition, he willed DFl. 30.000 to the library of that department after the eventual demise of his wife, but she decided to donate DFl. 25.000 directly to the Royal Academy of Sciences instead (Tammenoms Bakker 1934).

His wife, Henriette Heymans, saw to it that he could do his work without interruptions. His private life is practically a *terra incognita*. He preferred music, art and doing sports.

Wertheim Salomonson suffered from angina pectoris; his death on 16 September 1922 was probably caused by a myocardial infarction. A few days before, he, as Rector Magnificus, addressed the university's corpus academicus, on the annual Rectorate's transmission. The summer of 1922, he had obtained much relief during a 'cure' treatment in Nauheim (Germany). Two attacks of angina pectoris on the day preceding his death heralded the close of his life. His wife survived him for a quarter of a century (9 August 1948).

At the 25th anniversary celebration of the Society for Electrology and Roentgenology (7 November 1926) a foundation was established to honour the pioneer of roentgenology and to have a medal coined to promote the science of roentgenology. Both the foundation and the medal carry his name.

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C. Winkler *1855-1941* 30

P.J. Koehler

Cornelis Winkler may probably be considered the father of Dutch neurology or at least the godfather, as he was not a professor of neurology (see Brouwer, chapter 19), but took the combined chair of Psychiatry and Neurology (Utrecht, 1893). For many years he had struggled for the inclusion of psychiatry and neurology in the *series lectionum* of the medical faculties. Eventually, chairs of psychiatry and neurology were gradually founded, starting with his own chair in Utrecht in 1893. It took even longer before university clinics for psychiatry and neurology were established. In comparison to the German universities, the main point of reference for Dutch psychiatry and neurology, the establishment of chairs and clinics was a rather long process.

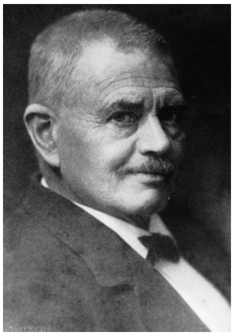

Figure 1. Cornelis Winkler (1855-1941).

Cornelis Winkler was born on February 25, 1855 in Vianen, a town on the river Lek, close to Utrecht, in the centre of the Netherlands. His great-grandfather, grandfather and father, Daniël Gualtherus, had been physicians. Daniël G. married Cornelia Gerarda van Tienhoven and they had six children, the eldest of whom was Cornelis. As a child, Cornelis was interested in nature, studying small animals he found in the neighbouring meadows. He went to high school (HBS) in Amsterdam and he returned to Utrecht in 1873 for his medical studies. He was influenced by the famous Franciscus Cornelis Donders (1818 - 1889), one of the first authoritative physicians in the Netherlands to adhere to the scientific method in medicine. Donders taught physiology as well as ophthalmology; practical ophthalmology being taught by Herman Snellen Sr. (1834-1908). He was also influenced by the other physiologist of the time, Donder's son-in-law, Theodore Engelmann (1843-1909). Winkler wrote his thesis on *Virus tuberculosum* (1879). Following graduation, he became resident at the Municipal Hospital in The Hague at a time when aseptic wound treatment was being introduced. However, after a while he decided to write to some of his professors in Utrecht, as he preferred to do research. Donders invited him to become reader of psychiatry, but Winkler declined. He was not very enthusiastic about psychiatry, which seemed to be too far remote from medicine. On the other hand, he was interested in neurology and wished to treat patients with nervous diseases. Donders accepted his decision and Winkler became assistant at the outpatient clinic of S. Talma (1847-1918), professor of internal medicine. In this function he had enough time to perform research.

Winkler had been impressed by the results of the electrical stimulation experiments on the cortex of dogs by Gustav Fritsch (1838-1927) and Eduard Hitzig (1838-1907) in Berlin (1880). Winkler planned to repeat the stimulation experiments and perform ablation experiments in Utrecht. In 1882 he visited Vienna to meet Theodor Meynert (1833-1892), who had impressed him and whom he considered founder of scientific psychiatry. He also visited the Landes-Irrenanstalt where he met Julius Wagner von Jauregg (1857-1940) with whom he became friends. He told him that he had refused to become reader in psychiatry because this science was based too much on philosophy and psychology. Wagner von Jauregg, an adherent to the German neuropsychiatry school, however, believed that psychiatry could be taught from a physiological as well as a neurological point of view and advised Winkler to try to get psychiatry and neurology in one hand and if possible to teach them both. After returning to the Netherlands and discussing the ideas with Donders, he finally became reader of psychiatry in Utrecht (1885). In that year he also visited Baden and Heidelberg and met Ludwig Edinger (1855-1918), Carl Weigert (1845-1904) and Hitzig. He visited Bernhard von Gudden (1824-1886) in München, who advised him how to organise his future position, in particular with respect to experimental anatomy (Winkler 1982, p. 49). After these encounters, it is no surprise to learn the title of his inaugural address of October 5th 1885: 'Psycho-pathology as brain pathology between the clinical sciences'. 'Brain psychiatry', in the tradition of Wilhelm Griesinger (1817-1868; 'Geisteskrankheiten sind Hirnkrankheiten'), Meynert and Wernicke, who he often mentioned as his examples, had found a new supporter and important representative in the Netherlands.

In 1886, Winkler interrupted his work and travelled to the Dutch East Indies, to investigate the cause of beriberi, in cooperation with Cornelis Pekelharing (1848-1922) and Christiaan Eykman (1858-1944). Back in Utrecht at the end of 1888, Winkler married Catharina Wilhelmina Pelgrim and continued his neuroanatomical work, performing cortical ablation experiments in rabbits and dogs.

In 1893, a chair of psychiatry and neurology was created for him at the Utrecht Faculty of Medicine and plans for building a clinic were made. Demonstrating Winkler's most important concern in this period, his inaugural lecture was entitled 'On the significance of teaching psychiatry for medicine' (1893). As he did not have a clinic at his disposal, but only a small room in which there was scarcely space for 25 students, Winkler resigned in 1896 and accepted the new chair of Neurology and Psychiatry at the University of Amsterdam. A neurological service had been present in Amsterdam for several years when Winkler arrived. Gerrit Waller (from 1874-1883), Constant Charles Delprat (1854-1934; from 1883-1893), and Johannes K.A. Wertheim Salomonson (1864-1922; starting in 1893)), residents of Pieter Klazes Pel (1852-1919), professor of internal medicine, had worked at the electro-therapeutic outpatient clinic. Winkler now acquired a neurological clinic, originally Hertz's internal clinic, at the Binnengasthuis, and a psychiatric clinic at the Buitengasthuis. In 1899, he succeeded in having an extra-ordinary chair of neurology and electro-therapy created for Wertheim Salomonson. Roentgenology was added to the assignment in the subsequent year.

Winkler was nominated a member of the physical section of the Royal Academy of Sciences in 1898. Several physicians prepared their theses under his guidance, one of them being G. van Rijnberk, who studied the dermatomal innervation of the skin and who was to become professor of physiology,. In this period, the student C.U. Ariëns Kappers also worked with him and won a contest on the development of the Schwann sheath.

Winkler's wife died from an incurable disease in 1903. Their oldest child was barely 13 years old and in the following year, Winkler also took the three children of his wife's brother into his home when both their parents died. Now he had to care for seven children. For obvious reasons, he became more interested in children's education in this period and held a few lectures in educational circles. Despite the domestic problems, he gradually took up his scientific duties again, resulting in theses on multiple sclerosis (M. Sträter), M. Parkinson (G.W. Manschot), and the central optic system (K.H. Bouman). In 1906 he remarried, to E.C. Junius, who had worked in his laboratory. The family moved from Oosteinde to the Heerengracht, where he had a large study that accommodated his large library.

In cooperation with Wayenburg and Wertheim Salomonson, Winkler organised the international congress for neurology, psychiatry and mental care in 1907 in Amsterdam. He invited Richard Ewald together with his wife, who stayed at his home. Furthermore, he met Arthur van Gehuchten, Arnold Pick, Hugo Liepmann and Constantin von Monakow. He remained a friend with the latter for the rest of their lives. Numerous letters from their correspondence are kept at the Medizinhistorisches Institut in Zurich (Koehler and Jagella 2002a,b). In his autobiography, Winkler wrote that this congress divided his life into two parts. From that moment onwards, he focussed on anatomical-clinical work (Winkler 1982, p. 115).

In 1908, Winkler debated on his views that women cannot regularly perform intellectual work because of their sensibility, subjectivity, motherhood, and the way they differ psychologically from men. Challenged by the gynaecologist Treub, he opposed the advocate of women's rights, Dr. C van Tusschenbroek in a debating session (Winkler 1982, p. 98-99).

Winkler was one of the founders of the Society of Amsterdam Neurologists in 1909, the most influential forum for neurological science in the Netherlands. In the same year the Central Institute for Brain Research in Amsterdam was opened, following a report written by Winkler and Bolk (Winkler 1909a; see chapter on extra-academic centres). Many renowned neuroscientists came to Amsterdam to attend the opening. Camillo Golgi stayed at Winkler's home.

Scientific research became concentrated on neuroanatomical subjects. Several residents wrote their Ph.D.-degrees on this subject. Dr. Ada Potter wrote *An anatomical guide to experimental researches of the rabbits brain* (1911), an impressive project that received wide recognition. A few years later she cooperated in the production of an atlas of the cat's brain (1914). The Brain Commission commissioned the production of an atlas of the human brain. The intention was that Winkler and Genosuke Fuse, assistant of von Monakow, would each carry out a part of the project, which is why

Winkler had to travel to Zurich several times, and von Monakow visited Amsterdam on several occasions. The pons and medulla oblongata would be analysed in Amsterdam, whereas the mesencephalon would be dissected in Zurich. Both laboratories started on the brain of a one-year old child in 1914. However, because of the outbreak of World War I, the project was never completed.

Domestic misfortune struck again, when Winkler's daughter died, and his oldest son from his second marriage suffered from encephalitis, rendering him mentally handicapped. In 1911, Winkler was nominated rector of the University of Amsterdam. However, he continued his neuroanatomical work and travelled to Frankfurt to meet Ludwig Edinger (1855-1918), and to Heidelberg, where he met Franz Nissl (1860-1919), who impressed him by the huge collection of slices of the central nervous system.

While Winkler tried to obtain a new building for the neurological and psychiatric clinic on the site of the Wilhelmina Gasthuis, plans were postponed because of the war. In the meantime, Winkler was called to Utrecht to succeed Karl Heilbronner (1869-1914), who had recently died. A new, modern psychiatric-neurological clinic, including a laboratory, had been built under Heilbronner, and although Winkler was almost sixty years old, he returned to Utrecht (1915), where he would have one of the best equipped psychiatric-neurological clinics of Europe at his disposal. The Utrecht clinic included a radiological department, for which Winkler asked Hendrik Willem Stenvers (1889-1973) to become the superintendent. In this period Winkler started his *Handbook of Neurology*, in which he planned to describe the anatomy of the nervous system in relation to the function. Finally, he would complete five volumes of the section on *The Structure of the Nervous System*, the first volume of which appeared in 1917 and the last in 1933. He was not able to complete the series with a sixth volume on the cerebral cortex, because of his age (78). In the correspondence with von Monakow, Winkler explained that the title was in fact the result of a misunderstanding with the publisher; the original plan had been to call the book *The Structure of the Nervous System* (Koehler and Jagella 2002b). It should have become a part of a larger multi-author project that was never carried out.

As for psychiatric teaching Winkler "kept as much as possible to the doctrines of Wernicke, i.e., I taught psychiatry on a biological basis" (Winkler 1982, p. 145). In this way, he opposed the new theories of Sigmund Freud. In his correspondence with von Monakow, Winkler's opinion is quite clear: "I was forced to form an opinion about Freud, so I had to make a study of the literature, and am now convinced that it is absolute rubbish" (transl. PJK from letter of 7/5/1917, Koehler and Jagella 2002b)

In 1918, at the 25th anniversary of Winkler's professorship, his colleagues and friends gave him the *Opera Omnia* in six volumes, and the Netherlands Society of Psychiatry and Neurology offered him a Festschrift. The *Opera Omnia* was later extended with three further volumes. In cooperation with the Dutch physician Th. Joekes, who lived in London, Winkler tried to improve international intellectual cooperation. Under the auspices of the Royal Academy an interchange commission was installed, which, from 1920 until 1928, organised a series of interchange-lectures at various universities. At such meetings, Winkler and other leading Dutch neurologists had ample occasion for discussions with Frederick Mott, Grafton Elliott Smith, Henry Head and Kinnier Wilson (Winkler 1982, p. 151).

After the decease of Wertheim Salomonson in 1922 and the subsequent division of Amsterdam neuropsychiatry into two chairs, one of neurology for Bernard Brouwer, and one of psychiatry for K.H. Bouman, Winkler admitted that: "Whereas it had been necessary to keep psychiatry and neurology in one hand in 1890, it was now mandatory to demand a separate chair for neurology, considering the enormous flight this science has experienced" (p. 153).

Winkler presented his farewell address on July 20, 1925, entitled: 'On the future of psychiatry'. From his comments on this lecture we know whom he held in esteem in neurology and psychiatry. "Charcot and Meynert coupled psychiatry to neurology and demanded an anatomical foundation. Wernicke even demanded the assistance of the localisation-hypothesis in order to explain psychological phenomena. Proceeding on the way taken by Hughlings Jackson, Sherrington taught that higher functions, notably the integral summation of various reflexes are already realised in the spinal cord" (Winkler 1982, p. 154). To this list of favourite neurologists, he added Rudolf Magnus (1873-1927), whose publication *Körperstellung* had recently appeared. These were the persons who worked from the basis to the top. Among the scientists who worked 'top-down', he mentioned Ambroise Auguste Liébault (1823-1904) and Hyppolyte Bernheim (1837-1919) on hypnosis, and furthermore Pierre Janet (1850-1947), Sigmund Freud (1856-1939) and Karl Jaspers (1883-1969). Winkler did not appreciate this method and held on to his standpoint that psychiatry should never break away from brain pathology (Winkler, p. 155).

Winkler was disappointed about the appointment of Leendert Bouman as his successor at the chair in Utrecht. He had hoped to be succeeded by Christiaan van Valkenburg, as Bouman was more dedicated to a different direction of neuropsychiatry. Despite the tension between the two, Bouman offered him a room at the clinic to continue his neuroanatomical work. Winkler's wife worked alongside him in the lab, studying pathological neuroglia. Since he had more spare time now, he was able to go to Zurich and meet von Monakow every year. When von Monakow retired in 1927, the deanery asked Winkler's advice about the successor. Together they tried to get Van Valkenburg, who was second on the list of nominees, but ultimately Mieczyslaw Minkowski (1884-1972) was chosen. That Winkler's friendship with von Monakow was valuable to him is clear from the lines he wrote when the latter died in 1930: "I miss a faithful friend in him, and the often fruitful exchange of ideas certainly had a stimulating effect on my work" (Winkler 1982, p. 163). From the correspondence with von Monakow we may conclude that Winkler was probably inspired to write an autobiography, after reading and commenting on von Monakow's manuscript of *Vita Mea* in 1927 (von Monakow 1970).

Figure 2.
The Utrecht laboratory (around 1918). From left to right Winkler's second wife Winkler-Junius (whom he married in 1906 following the decease in 1903 of his first wife), Winkler, Miss Uiterwaal (laboratory assistant), Dr. Faber, Mrs. Pameyer (resident).

Winkler's work

Leafing through Winkler's *Opera Omnia* it appears that one of the subjects he often wrote about is the teaching of psychiatry (and neurology) at the universities. In the early 1890s, Winkler started his struggle to have psychiatry examined for medical graduation (Winkler 1890a). A request addressed to the Netherlands Society of Medicine (NMG) was rejected, despite Winkler's endeavours. The opponents argued that the medical curriculum was already too full. Winkler, however, feared for the future of neurology, which he wanted to teach together with psychiatry, and which was presently given by internal clinicians: "... neurology might be strangled to death between the internal clinic and psychiatry..." (Winkler 1982, p. 82).

A major part of his work concerned (experimental) neuroanatomy. He often applied Von Gudden's atrophy method to study the course of nerves in the central nervous system. Many of the theses of Winkler's pupils were written on neuroanatomical subjects. Clinical subjects were studied as well, including syringomyelia (by A. Bosch 1895), aphasia (by M.A. van Melle 1900), paralysis agitans (by G.W. Manschot 1904), the plantar reflex (by W. van Woerkom 1910) (Anonymous 1918, Winkler 1982). His work on the central course of the eighth cranial nerve has become well known; he proved that the acoustic and vestibular parts do not follow a completely separate course (Winkler 1890b, 1905, 1907a). The afore-mentioned five-volume

Handbook of Neurology is also a product of his work on the structure of the nervous system. In cooperation with his pupil Van Rijnberk, he worked on the segmental sensory innervation (Winkler and Van Rijnberk 1901-3, Winkler 1903, Winkler and Van Rijnberk 1910).

Winkler performed brain surgery for tumours, abscesses and haemorrhages, together with the surgeon Johan Anton Guldenarm (1852-1905). Winkler's experience at the surgical department in The Hague was opportune in this respect. He published several papers on cranial surgery in cooperation with Guldenarm (Winkler et al. 1890, Winkler 1894), including papers on epilepsy surgery (Winkler 1897b).

Several papers deal with aphasia and functional localisation (Winkler 1902, 1909b). He chose this subject for his address at the *dies natalis* in 1912 (Winkler 1912). With respect to function localisation he adhered to von Monakow's ideas, including diaschizis as a model for function substitution following lesions. He objected to rigorous localisation of all functions, in particular cognitive functions. Furthermore, he opposed the neuron-theory (Cajal) in favour of the reticular theory (Golgi), as this better explained his histological and experimental neuroanatomical findings (Koehler and Jagella 2002b).

As a psychiatrist he preferred to approach the subject from a material point of view. He tried to explain psychiatry from the basis of neuropathology, being a scientific man in heart and soul. In his view, the scientific method should explain neurological as well as psychiatric phenomena. In this way it is not difficult to recognise the influence of the German-Austrian neuropsychiatrists, e.g., Meynert and Wernicke, whom he admired, as well as those whom he met at the beginning of his career (Winkler 1900). He was critical with respect to Freud and psychoanalysis (Winkler 1917).

Figure 3.
Winkler and his wife in old age.

Following his retirement in 1925, he continued working on his *Handbook of Neurology*, the third volume of which was published one year later and the last in 1933, when Winkler was 78 years old. He enjoyed a quiet life with his wife for eight years, up to his death in 1941 (fig. 3).

Note

[1] For biographical data the following sources were used: Pekelharing 1918, Prick 1978, Lhermitte and Mourgue, 1946, Brouwer 1941, Van Valkenburg 1955, Stenvers 1955 and Winkler 1982.

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Index