Alois Alzheimer (1864-1915)

Manuel B. Graeber

University Department of Neuropathology, Imperial College London and Hammersmith Hospitals Trust, London, UK

Alois Alzheimer (Fig. 1) was born on the 14th of June 1864 in Marktbreit am Main (Germany) and died in Breslau (now Wroclaw, Poland) on December 19, 1915. Alzheimer's most widely known contribution to the Neurosciences is the histological description of the disease that was named after him by Emil Kraepelin (1). However, research into this disease represents but a small segment of Alzheimer's clinico-pathological interests which were focused on the histopathology of the cerebral cortex in the mentally ill.

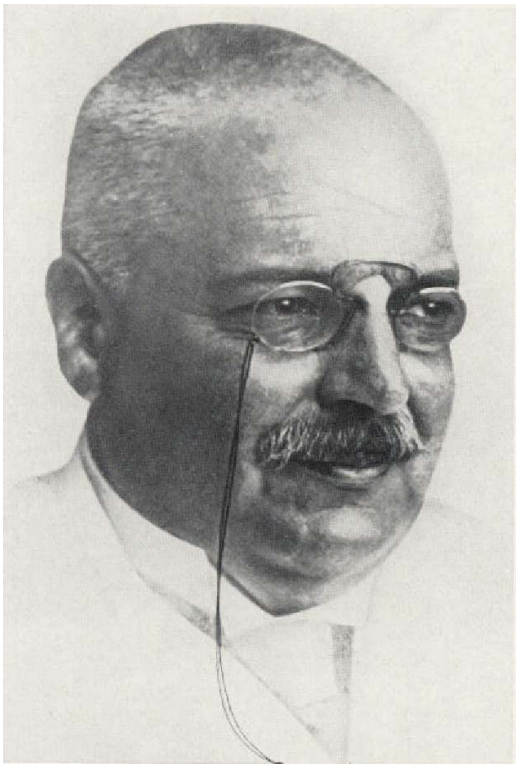


Figure 1 *Alois Alzheimer. The original of this protrait is kept in the historical library of the Max-Planck-Institute of Neurobiology (formerly the Theoretical Institute of the Max-Planck-Institute of Psychiatry, Munich), Martinsried, Germany*

Through his early histopathological research in psychiatry, Alzheimer became one of the founding fathers of neuropathology, nurturing a unique brain research tradition in Germany that lasted for almost a century[1]. Alzheimer always thought of himself as a physician and was able to combine his innovative research with the demanding clinical duties of a psychiatrist.

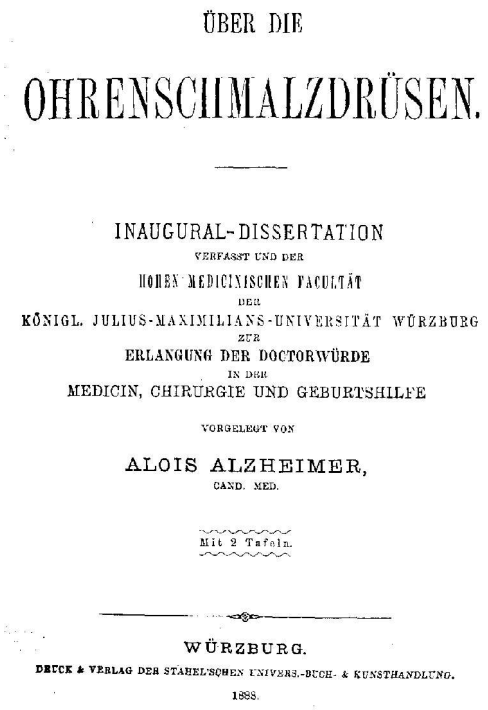
The Man

His colleagues had a high esteem for Alzheimer's work and also for his personality. In his obituary for Alzheimer, Robert Gaupp, then head of psychiatry at Tübingen University and Alzheimer's predecessor as Oberarzt[2] in Kraepelin's clinic in Munich, the Royal Psychiatric Hospital, wrote: "… Alzheimer was a man with a clear head and unusual creative powers who took greatest pains over his work and had a strong sense for scientific truth. The right training provided, this combination of talents had to result in outstanding achievements in the field of science. This was complemented by his warmhearted interest in the fellow man, his mentality of a true physician, and the great enjoyment from combining science and medical practice. Although he mainly worked in a small, infinitely difficult specialist field, he always made sure that his research could not endanger the clinician and physician in him" (4).

It was in Kraepelin's clinic in Munich where Alzheimer's life as a scientist came to full fruition. Alzheimer himself provides a short account of his professional development until he moved to Munich in 1903. In his curriculum vitae, written in the same year, he states: "The undersigned, Dr. med. Alois Alzheimer, catholic, born at Marktbreit in Bavaria on the 14th of June 1864 as son of the Royal notary, Eduard Alzheimer, attended the elementary school at Marktbreit, the Gymnasium[3] at Aschaffen-burg and the Universities of Berlin, Tübingen and Würzburg. In 1887, he passed the doctoral exam in Würzburg (Fig. 2), and in the following year the state examination. Subsequently, he continued working in

1 This tradition has become known as the "Munich School of Neuropathology". Nissl, Alzheimer and Spielmeyer are credited for its creation (2). It ended with the closure of Georg Kreutzberg's Department at the Max-Planck-Institute of Neurobiology in 2000; for additional historical information see ref. 3.
2 Senior physician
3 Secondary school

Würzburg for a few months in the histological laboratory of Geheimrat[4] von Koelliker, and worked then for seven years as assistant physician and seven years as second physician[5] in the municipal mental asylum in Frankfurt/Main. In order to be able to devote more time to scientific studies, he left this position in March 1903 after the



ÜBER DIE

OHRENSCHMALZDRÜSEN.

INAUGURAL-DISSERTATION

VERFASST UND DER

HOHEN MEDICINISCHEN FACULTÄT

DER

KÖNIGL. JULIUS-MAXIMILIANS-UNIVERSITÄT WÜRZBURG

ZUR

ERLANGUNG DER DOCTORWÜRDE

IN DER

MEDICIN, CHIRURGIE UND GEBURTSHILFE

VORGELEGT VON

ALOIS ALZHEIMER,

CAND. MED.

Mit 2 Tafeln.

WÜRZBURG.

DRUCK & VERLAG DER STAHEL'SCHEN UNIVERS.-BUCH- & KUNSTHANDLUNG.

1888.

Figure 2 *Alzheimer's doctoral thesis on the earwax glands (Würzburg, 1888)*

Hofrat[6], Professor Kraepelin, promised him a post as scientific assistant in his clinic in Heidelberg. Together with Professor Kraepelin he moved to Munich in October of this year." (5)[7]

While the decade in Munich brought out the master of neurohistological technique in Alzheimer, his 14 years in Frankfurt (1888-1902) have to be considered foundation years and three aspects seem of particular importance: Firstly, after joining the clinical service run by Professor Emil Sioli at the Frankfurt Asylum, Alzheimer found himself in a unique position. He was, at the same time, able to contribute to the development of a modern clinical service while setting up a scientific patient database. In addition, he built an archive of autopsy cases, on which he could rely during the rest of his scientific career. For instance, the brain of the first Alzheimer disease patient, Auguste D., who died in Frankfurt in 1906, was sent to Alzheimer when he was already in Munich, i.e. four years after he had left Frankfurt. Secondly, Alois Alzheimer met Franz Nissl in Frankfurt. Only four years older, Nissl had already established himself in the new field of neurohistology. Nissl was widely known for his revolutionary "Nissl staining" method for nerve cells (6) which is still in use in routine and experimental neurohistology laboratories around the world. Nissl arrived in Frankfurt shortly after Alzheimer and received an appointment as second physician[5] in Sioli's clinic. Alzheimer and Nissl became close friends and spent much time together discussing findings over the microscope. Nissl's influence on Alzheimer's work cannot be overestimated (7). Thirdly, in 1894 Alzheimer married his beloved wife Cecilie Geisenheimer (neé Wallerstein) in Frankfurt. This marriage provided Alzheimer with financial independence and put him in a position to support his own research.

Immediately after his move to Munich, Alzheimer published his habilitation thesis[8] on the histopathology of general paralysis of the insane ("Progessive Paralyse", Fig. 3; and see ref. 8). This late complication of a syphilis infection was very common in Alzheimer's time: about 10% of all hospitalised psychiatric patients suffered from the disease. Alzheimer was able to study a series of 170 autopsy brains providing the histological knowledge available on the disease today.

Alzheimer's newly founded "neuro-anatomical laboratory" in Munich won international acclaim resulting in a large number of international visitors. The long list of names includes N. Achucarro (Spain), F. Bonfiglio (Italy), S. Casamajor (USA), U.

4 Privy councillor

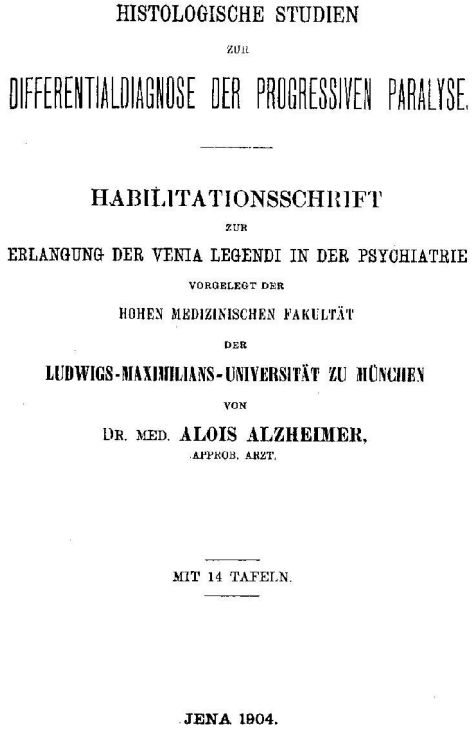
5 Oberarzt, lead clinician under the Professor; from 1896, as successor to Franz Nissl who had left for Kraepelin's clinic in Heidelberg to prepare his habilitation (see footnote 8)

6 Privy Councillor, honorary

7 This article contains a photo of Alzheimer's Curriculum vitae written in "old German" (before Sütterlin)

8 A habilitation thesis was a formal requirement for a promotion to the rank of professor in the German academic system

Cerletti (Italy), H.G. Creutzfeldt (Germany), B. Doinikow (Russia), A Farworsky (Russia), F. Fulci (Italy), A. Jakob (Germany), F. Lotmar (Switzerland), L. Merzbacher (Argen-tina), L. Omorokow (Russia), G. Perusini (Italy), St. Rosental (Poland) and T. Simchowicz (Poland) (5).



HISTOLOGISCHE STUDIEN

ZUR

DIFFERENTIALDIAGNOSE DER PROGRESSIVEN PARALYSE.

HABILITATIONSSCHRIFT

ZUR

ERLANGUNG DER VENIA LEGENDI IN DER PSYCHIATRIE

VORGELEGT DER

HOHEN MEDIZINISCHEN FAKULTÄT

DER

LUDWIGS-MAXIMILIANS-UNIVERSITÄT ZU MÜNCHEN

VON

DR. MED. ALOIS ALZHEIMER,

APPROB. ARZT.

MIT 14 TAFELN.

JENA 1904.

Figure 3 *Alzheimer's habilitation thesis on general paralysis of the insane (Munich, 1904)*

There are reports that Alzheimer's laboratory had an unusually warm atmosphere that was highly conducive to learning and creative research. As K. Kleist (5) described it, Alzheimer would return from his lunch break at 2 pm every day, one hour earlier than his collaborators, and resume his work in the laboratory. When his co-workers later joined him, he would walk by every seat smoking his cigar and explain to them with great patience subtle neuromorphological details through the microscope.
It is of note that F.H. Lewy, who discovered the Lewy bodies in Parkinson's disease, was one of Alzheimer's visiting researchers. Lewy published his seminal observations on Lewy bodies under the Munich laboratory address. Alzheimer must have had a very high opinion of the young doctor as he selected the 27 year old Dr Lewy to run his research laboratory in Breslau. It was very unfortunate for Lewy that Alzheimer died three years after taking up the chair in Breslau. Lewy paid the Munich laboratory another visit a number of years later when Walther Spielmeyer had succeeded Alzheimer as director of the world famous laboratory.

Alzheimer's boss, Emil Kraepelin, was an early founder of modern psychiatry and a visionary who propagated the idea of a biological cause of psychiatric diseases at a time when Freud was preaching psychoanalysis. He is best known for his work on schizophrenia. Kraepelin created an environment where Alzheimer and other brain researchers could excel. Apart from Franz Nissl, who even gave up his chair of psychiatry in Heidelberg to conduct basic research in Kraepelin's institute, this group later also included Corbinian Brodman and Emil Jahnelt. Kraepelin was an astute politician who succeeded in raising funding for a new psychiatric research institute in the middle of World War I. The foundation of Alzheimer's research laboratory was a logical consequence of Kraepelin's original concept, but without Alzheimer's successful scientific work, Kraepelin would have hardly had a strong argument for the establishment of his research institute. The latter subsequently became the Deutsche Forschungsanstalt für Psychiatry, Kaiser-Wilhelm-Institut and, after World War II, was renamed the Max-Planck-Institute of Psychiatry.

The Work

Alzheimer's work has been reviewed in depth by his successor, Walther Spielmeyer, in a very impressive obituary (7) which appeared in a journal Alzheimer had founded[9]. The following text contains several translated passages and excerpts from this unique article.

According to Spielmeyer, Alzheimer's research was characterised by a close co-operation between the anatomical sciences and the clinic. His histological research was guided by clinical aspects and clinical experiences, and, in turn, clarification of

9 See ref. 4, not to be confused with the journal shown in Figure 4

clinical problems through scrutiny of anatomical facts was a most important scientific goal. Kraepelin saw this as a key reason for Alzheimer's importance and the great success of Alzheimer's work. It is not surprising that Alzheimer considered "case reporting" an important scientific activity. He explicitely stated that anatomical research needs to be guided by clinical experience. This concept is readily apparent from a number of his publications (cf. Appendix). Alzheimer's large study on general paralysis of the insane (8) is an excellent example. Starting out from clinically typical cases, the characteristic histological features are determined, novel histological observations are compared with those in other diseases, and Alzheimer then demonstrates how the histological differential diagnosis can be

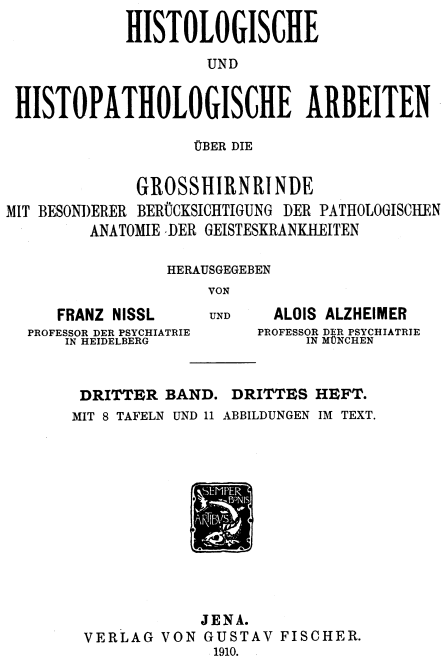

HISTOLOGISCHE
UND
HISTOPATHOLOGISCHE ARBEITEN
ÜBER DIE
GROSSHIRNRINDE
MIT BESONDERER BERÜCKSICHTIGUNG DER PATHOLOGISCHEN ANATOMIE DER GEISTESKRANKHEITEN
HERAUSGEGEBEN
VON
FRANZ NISSL UND ALOIS ALZHEIMER
PROFESSOR DER PSYCHIATRIE IN HEIDELBERG
PROFESSOR DER PSYCHIATRIE IN MÜNCHEN
DRITTER BAND. DRITTES HEFT.
MIT 8 TAFELN UND 11 ABBILDUNGEN IM TEXT.
JENA.
VERLAG VON GUSTAV FISCHER.
1910.

Figure 4 *The Journal founded and edited by Nissl and later by Nissl and Alzheimer*

used to answer clinical questions. According to Spielmeyer, Nissl and Alzheimer won the "victory of anatomy in psychiatry" (7). The scientific activity of both researchers had an emphasis on the pathology of the cerebral cortex in mental diseases quite in line with Kraepelin's concept for psychiatry (Fig. 4).

Alzheimer's early research benefited from the fact that when he was a young doctor in Professor Sioli's asylum, experienced colleagues such as Weigert and Nissl were also in Frankfurt. By 1884, Weigert published his technique for the visualisation of myelin sheaths, and Nissl developed his famous method for the detailed morphological analysis of nerve cells. Spielmeyer emphasises the great influence Nissl had on Alzheimer. Alzheimer and Nissl did research together over many years in Frankfurt and extended their close friendship and scientific collaboration in Heidelberg where Alzheimer worked as an assistant at Kraepelin's clinic between 1902 and 1903. Nissl's strong influence on his work was acknowledged by Alzheimer in the following beautiful manner (7): "I shall mention Nissl's name as often as scientific works by him on the topic under discussion are known to me. However, Nissl's share in these studies does not end with that. The amicable scientific interactions which I was allowed to entertain with him over the last 15 years have given me so much stimulation that I must concede – to give but one example – that none of the following ideas that might enhance our knowledge has been conceived without his direct or indirect participation."[10]

Alzheimer's work on general paralysis of the insane is among his best known publications. Spielmeyer suggests that any research on cortical pathology has to start with a review of Nissl's studies but also of this basic publication (8) of Alzheimer's. For the latter study, Alzheimer had examined 170 cases of general paralysis of the insane, illustrating how common the disease was at the time. Importantly, in this study Alzheimer realised that the degenerative process which underlies this devastating illness takes place rather independently from the inflammatory reactions. However, the exact nature of the disease process has remained enigmatic. As Spielmeyer pointed out (7), very little of Alzheimer's teachings had to be revised and, though 100 years old today, they have not been corrected or amended but only confirmed.

10 This is from a footnote on page 20 of ref. 8. There is one more sentence in the original: "This does not preclude the fact that Nissl may well disagree with some views expressed here." ("Das hindert nicht, daß vielleicht Nissl manche Auffassungen, die hier wiedergegeben sind, nicht teilen dűrfte".)

Alois Alzheimer (1864-1915)

Working on general paralysis as a “model” cortical disease, Alzheimer delineated senile dementia, cerebral atherosclerosis, damage caused by chronic alcoholism and acute syphilitic infections of the brain. Furthermore, lyssa, trypanosomiasis and the anatomical basis of idiocy[11] were among his interests. Alzheimer further recognised the neoplastic nature of the tumourous "glia masses" in tuberous sclerosis, and he also worked on the anatomical basis of Huntington’s chorea and the choreatic movements in general. In hepatolenticular degeneration, Alzheimer described glial changes which now carry his name, Alzheimer type 1 and 2 astrocytes[12].

Atherosclerosis had been of interest to Alzheimer since the start of his scientific work. Between 1894 and 1902, he acquired detailed knowledge on the subject.

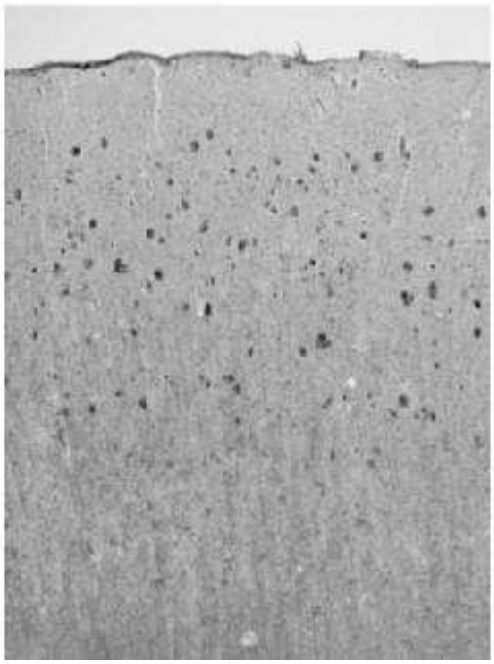
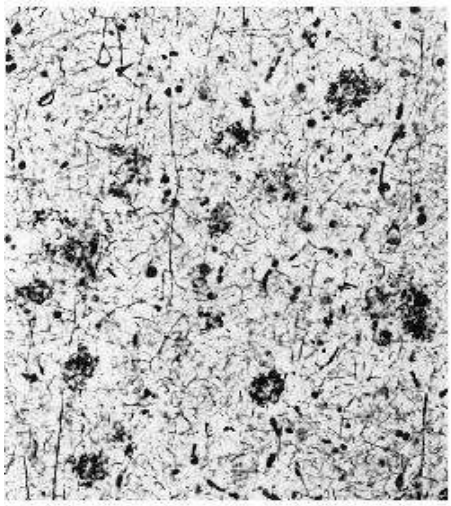


Figure 5 *Alzheimer’s disease. Amyloid plaques predominantly in the upper cortical layers of Auguste D.’s (9) brain as described by Alzheimer (10) (from ref. 11)*

Alzheimer went on to demonstrate that Binswanger’s "Encephalitis subcorticalis chronica" was not inflammatory in nature. His studies on atherosclerosis led Alzheimer to investigate other senile processes and notably dementia. Alzheimer’s studies on the pathology of the cerebral cortex culminated with the publication of his now famous short article providing the first description of the neurofibrillary tangles in the first Alzheimer patient, Auguste D. (10) (Figs. 5-8). In a later, more comprehensive review article that was published in 1911, Alzheimer discusses various aspects of the disease (12). It may come as a surprise to many today that it was already clear at Alzheimer’s time that there



Figures 6 and 7 *Amyloid plaques at higher magnification (from ref. 13)*

11 Extreme mental retardation
12 See neuropathological textbooks for further explanation

are no fundamental differences between the histological substrate of the classical (presenile) form of Alzheimer's disease and senile dementia. Alzheimer himself viewed classical (presenile) Alzheimer's disease as an atypical form of senile dementia (7). Alzheimer's work answered the important question of whether the senile dementing process depends on atherosclerosis or other regressive vascular changes. It became clear that cerebral atherosclerosis and senile dementia are fundamentally different diseases.

Epilepsy forms part of another large disease group Alzheimer worked on to define anatomical subtypes. He stated: "If we aim to understand the nature of a disease, to predict its prognosis, to elucidate its course and finally treat it prophylactically or therapeutically, we must have clear, precisely defined disease entities before us. What we call epilepsy today, however, does not represent such an entity but apparently encompasses a whole group of different disorders." Alzheimer correctly pointed out that many cases of epilepsy show sclerotic changes of the "Ammonshorn". He also emphasised the importance of studying the breakdown of nervous tissue and the types of acute neuroglial responses in epileptic brains.

A review of his life's work reveals that there were two main periods of Alzheimer's scientific activity. The first period ended with his habilitation in 1904 and the publication of the corresponding article on general paralysis (8). After he had moved to Munich, Alzheimer wrote that in a few promising early instances, pathological anatomy had successfully demonstrated that diseases characterised by dementia and paralysis, respectively, may be caused by *different* tissue processes (7). This was important as Wernicke had proposed that "mental diseases with an anatomical correlate" may be caused by essentially the same disease process. Thus, the responses of the neuroglia would differ only in quantitative terms and disease-associated changes of the neurons would also not show alterations truly characteristic of the respective disease process. Alzheimer, however, demonstrated clearly that neither the pathological phenotype profile of a case nor the accompanying glial response manifest themselves as simple quantitative phenomena. Therefore, Alzheimer believed it to be a prime task of the "cortical anatomist" to determine the neuromorphological specifics of a disease process and to document all subtle differences in comparison to other cortical pathologies. Fortunately, Alzheimer's extensive histological material of his two published Alzheimer cases is now accessible and will be made freely available to the general public in due course[13].

Figure 8 *A neurofibrillary tangle, first described by Alzheimer in Auguste D.'s brain (from ref. 13)*

This original research material beautifully demonstrates that the histological stains produced by Alzheimer's laboratory were of the highest quality, a prerequisite, in fact, for his meticulous tissue analyses. In particular, Alzheimer realised that the responses of the neuroglia are strongly dependent on the type and intensity of a disease process. Furthermore, he was aware of the diagnostic difficulties surrounding a claimed "specific histopathology" associated with schizophrenia and warned against any overinterpretation.

13 http://www.microglia.net/AD_100yrs_Book.html

Like many great scientists, Alzheimer had problems with the academic establishment of his time. Rumoured to be "only an anatomist", it was an inordinately long time before he was awarded a full professorship in recognition of his achievements. Looking at his published works (see Appendix) the rumour was obviously wrong. The synergies between Alzheimer's anatomical and clinical studies have fostered the development of psychiatry and notably neuropathology like very few other research programmes. Alzheimer is rightly considered a founding father of neuropathology and his life's achievements exemplify the strong roots this discipline has, and needs to have, in the clinical neurosciences.

"EXCESSIVE RESERVATIONS AND PARALYSING DESPONDENCY HAVE NOT HELPED THE SCIENCES TO ADVANCE NOR ARE THEY HELPING THEM TO ADVANCE, BUT A HEALTHY OPTIMISM THAT CHEERFULLY SEARCHES FOR NEW WAYS TO UNDERSTAND, AS IT IS CONVINCED THAT IT WILL BE POSSIBLE TO FIND THEM."

Figure 9 *Alzheimer's research motto*[14]

Alzheimer was an optimist. Difficulties stimulated him to find novel ways in new territories. He formulated his approach to research on the occasion of the 25th anniversary of Prof. Dr. Emil Sioli's directorship of the Frankfurt mental asylum (Fig. 9.; cited in ref. 7, originally from ref. 49 in the Appendix). Alzheimer was a meticulous worker and never published prematurely. During one of his rare visits to the neuroanatomical laboratory, Kraepelin commented that Alzheimer's neuroanatomical "mills would grind rather slowly" (5). Spielmeyer comments on Alzheimer's publication policy: "Alzheimer never had to fight for recognition for his research work. The clarity of his oral presentations and writings convinced even a distant observer about the importance of his results. At these times [!][15] of prolific publishing[16] where everyone believes to have something of importance to say and where many advertise the little things they find over and over again, Alzheimer never took the floor unless he had something truly important to say." The scientific enterprise has continued to move forward since then and the result speaks for itself: as of September 2003, a search of the Medline database retrieves > 40,000 entries containing the term "Alzheimer", and a Google search yields 2,070,000 hits. A complete list of Alzheimer's published works is attached to this article (see Appendix).

14 "(Denn) nicht übermässige Bedenken und lähmende Verzagtheit helfen den Wissenschaften vorwärts und haben ihnen vorwärts geholfen, sondern ein gesunder Optimismus, der in froher Zuversicht nach neuen Wegen der Erkenntnis sucht, da er überzeugt ist, dass sie zu finden sein werden".

15 Spielmeyer wrote this in 1916 (7)

Acknowledgements

I am indebted to Karin and the late Johanna Stöltzing for their help with deciphering Alzheimer's handwritten Curriculum vitae. Special thanks go to Ingrid Holzinger and Dr James Chalcroft, Max-Planck-Institute of Neurobiology, Martinsried, Germany, for a scan of Alzheimer's portrait (Figure 1) and for help (I.H.) with obtaining several of Alzheimer's publications. Furthermore, I am grateful to Emilie M. Croisier, London, Professor Richard B. Banati, Sydney, and Dr Stephen Gentleman, London, for comments on the manuscript. I would also like to take this opportunity to thank the OpenSource community for making the OpenOffice software package freely available, which was used for the preparation of this manuscript on a computer running GNU/Linux. The text of this publication is published under the ICDNS GPL (general public license, see www.ICDNS.org for further information).

I would like to dedicate this article to Professor Georg W. Kreutzberg, Munich, and to the memory of the "Munich School of Neuropathology".

Web links

1. A current international neuropathological consensus definition of Alzheimer's disease can be found at

www.ICDNS.org,

a web site of the International Society of

16 Original: Vielschreiberei

Neuropathology.

2. A book, "100 Years of Alzheimer's Disease", is scheduled to appear in 2006 and will be published under a general public license. The book will illustrate all (>400) histological tissue sections used by Alzheimer for his research into the disease that was named after him, see

http://www.microglia.net/AD_100yrs_Book.html

Favourite Sentences

"Excessive reservations and paralysing despondency have not helped the sciences to advance nor are they helping them to advance, but a healthy optimism that cheerfully searches for new ways to understand, as it is convinced that it will be possible to find them."

References

1. Kraepelin E (1910) Psychiatrie. Ein Lehrbuch für Studierende und Ärzte. II. Band, Klinische Psychiatrie. Verlag Johann Ambrosius Barth, Leipzig
2. Spatz H (1961) Franz Nissl. In: Scholz W (ed) 50 Jahre Neuropathologie in Deutschland (1885-1935). Thieme, Stuttgart, pp 43-66
3. Graeber MB (1999) No man alone: The rediscovery of Alois Alzheimer's original cases. Brain Pathology 9:237-240
4. Gaupp R (1916) Alois Alzheimer. Münchener Medizinische Wochenschrift 6:195-196
5. Meyer JE (1961) Alois Alzheimer. In: Scholz W (ed) 50 Jahre Neuropathologie in Deutschland (1885-1935). Thieme, Stuttgart, pp 67-78
6. Kreutzberg GW (1984) 100 years of Nissl staining. Trends in Neurosciences 7: 236-237
7. Spielmeyer W (1916) Alzheimer's Lebenswerk. Zeitschrift für die gesamte Neurolologie und Psychiatrie 33:1-44
8. Alzheimer A (1904) Histologische Studien zur Differentialdiagnose der progressiven Paralyse. Nissl's histologische und histopathologische Arbeiten 1: 18-314
9. Maurer K, Volk S, Gerbaldo H (1997) Auguste D. and Alzheimer's disease. Lancet 349:1546-1549
10. Alzheimer A (1907) Über eine eigenartige Erkrankung der Hirnrinde. Allgemeine Zeitschrift für Psychiatrie 64:146-148
11. Graeber MB, Mehraein P (1999) Reanalysis of the first case of Alzheimer's disease. European Archives of Psychiatry and Clinical Neuroscience 249 Suppl 3:10-13
12. Alzheimer A (1911) Über eigenartige Krankheitsfälle des späteren Alters. Zeitschrift für die gesamte Neurologie und Psychiatrie 4:356-385
13. Graeber MB, Kosel S, Grasbon-Frodl E, Moeller HJ, Mehraein P (1998) Histopathology and APOE genotype of the first Alzheimer disease patient, Auguste D. Neurogenetics 1:223-228

Address of the author:

Manuel B. Graeber MD PhD MRCPath
Professor of Neuropathology
Honorary Consultant, Hammersmith HospitalsTrust
University Department of Neuropathology
Neurosciences Division, Faculty of Medicine
Imperial College London, Charing Cross Campus
Fulham Palace Road, London, W6 8RF, UK
m.graeber@imperial.ac.uk
www.graeber.net/manuel.html

Appendix

Publications of Alois Alzheimer (translated titles in italics)

1. Alzheimer A (1888) Ueber die Ohrenschmalzdruesen *[On the earwax glands].* Inaugural-Dissertation *[Medical doctoral thesis],* Koenigliche Julius-Maximilians-Universitaet Wuerzburg; 20 pages[17] and 2 plates with illustrations
2. Alzheimer A (1891) Ueber einen Fall von spinaler progressiver Muskelatrophie mit hinzutretender Erkrankung bulbaerer Kerne und der Rinde *[On a case of spinal progressive muscular atrophy with additional disease of bulbar nuclei and the cortex].* Archiv fuer Psychiatrie 23, 459; 27 pages and 1 plate with illustrations
3. Alzheimer A (1894) Die Paralysis progressiva der Entwicklungsjahre *[Progressive paralysis of adolescence].* Neurologisches Centralblatt 13, 732; 1 page
4. Alzheimer A (1894) Die arteriosklerotische Atrophie des Gehirns *[The arteriosclerotic atrophy of the brain].* Neurologisches Centralblatt 13, 765; 3 pages
5. Alzheimer A (1895) Kolloide Entartung des Gehirns *[Colloid degeneration of the brain].* Neurologisches Centralblatt 14, 886; 1 page
6. Alzheimer A (1895) Ueber die durch Druck auf den Augapfel hervorgerufenen Visionen *[On visual phenomena caused by pressure applied to the eye bulb].* Centralblatt fuer

17 Page and plate numbers are provided where possible

Nervenheilkunde und Psychiatrie 6, 473; 6 pages
7. Alzheimer A (1896) Die Fruehform der allgemeinen progressiven Paralyse *[The early form of general progressive paralysis]*. Allgemeine Zeitschrift fuer Psychiatrie 52, 533; 62 pages
8. Alzheimer A (1896) Ein „geborener Verbrecher“ *[A „born criminal“]*. Archiv fuer Psychiatrie und Nervenkrankheiten 28, 327; 27 pages
9. Alzheimer A (1896) Ueber die anatomische Ausbreitung des paralytischen Degenerationsprozesses *[On the anatomical spreading of the paralytic degeneration process]*. Neurologisches Centralblatt 15, 1007; 1 page
10. Alzheimer A (1896) Fuenf Faelle, in welchen sich neben einer hochgradigen Arterio-sklerose der Gefaesse disseminierte Herde in der Rinde, den Markleisten und im tiefen Mark finden *[Five cases in which, in addition to severe arteriosclerosis of the blood vessels, disseminated foci are found in the cortex, the cortical and the deep white matter]*. Ref.[18] Centralblatt fuer Nervenheilkunde und Psychiatrie 7, 549; 1 page
11. Alzheimer A (1897) Ueber rueckschreitende Amnesie bei der Epilepsie *[On retrograde amnesia in epilepsy]*. Centralblatt fuer Nervenheilkunde und Psychiatrie 8, 316; 2 pages
12. Alzheimer A (1897) Das Delirium acutum *[The acute delirium]*. Monatsschrift fuer Psychiatrie und Neurologie 2, 64; 2 pages
13. Alzheimer A (1897) Beitraege zur pathologischen Anatomie der Hirnrinde und zur anatomischen Grundlage einiger *Psychosen [Contributions to the pathological anatomy of the cerebral cortex and the anatomical basis of some psychoses]*. Monatsschrift fuer Psychiatrie und Neurologie 2, 82; 39 pages and 3 plates with illustrations
14. Alzheimer A (1897) Ein Fall von luetischer Meningomyelitis und –encephalitis *[A case of luetic meningomyelitis and –encephalitis]*. Archiv fuer Psychiatrie 29, 63; 17 pages and 1 plate with illustrations
15. Alzheimer A (1897) Ueber perivasculaere Gliose *[On perivascular gliosis]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medicin 53, 863; 3 pages
16. Alzheimer A (1898) Die Colloidentartung des Gehirns *[The colloid degeneration of the brain]*. Archiv fuer Psychiatrie 30; 37 pages and 1 plate with illustrations
17. Alzheimer A (1898) Ein Beitrag zur pathologischen Anatomie der Epilepsie *[A contribution on the pathological anatomy of epilepsy]*. Monatsschrift fuer Neurologie und Psychiatrie 4, 345; 25 pages and 2 plates with illustrations
18. Alzheimer A (1898) Neuere Arbeiten ueber die Dementia senilis und die auf atheromatoeser Gefaesserkrankung basie-renden Gehirnkrankheiten *[Newer studies on senile dementia and brain diseases caused by atheromatous vascular disease].* Monatsschrift fuer Psychiatrie 3, 101; 15 pages
19. Alzheimer A (1899) Beitrag zur pathologischen Anatomie der Seelen-stoerungen des Greisenalters *[Contribution on the pathological anatomy of the disturbances of the soul at high age]*. Neurologisches Centralblatt 18, 95; 2 pages
20. Alzheimer A (1900) Einiges zur pathologischen Anatomie der chronischen Geistesstoerungen *[On the pathological anatomy of chronic mental disturbances]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 57, 597; 3 pages
21. Alzheimer A (1902) Die Seelenstoerungen auf arteriosklerotischer Grundlage *[Disturbances of the soul caused by arteriosclerosis]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 59, 695; 17 pages
22. Alzheimer A (1902) Ueber atypische Paralysen *[On atypical paralyses]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 59, 170; 5 pages
23. Alzheimer A (1904) Histologische Studien zur Differentialdiagnose der progressiven Paralyse *[Histological studies on the differential diagnosis of progressive paralysis]*. Nissl’s histologische und histopathologische Arbeiten 1; 297 pages and 14 large plates with illustrations
24. Alzheimer A (1904) Histologische Studien zur Differentialdiagnose der progressiven Paralyse *[Histological studies on the differential diagnosis of progressive paralysis]*. Ludwig-Maximilians-Universitaet Muenchen *[Habilitation thesis]*
25. Alzheimer A (1904) Einiges ueber die anatomischen Grundlagen der Idiotie *[Some findings on the anatomical basis of lunacy]*. Centralblatt fuer Nervenheilkunde und Psychiatrie 15, 497; 9 pages
26. Alzheimer A (1904) Das Delirium alcoholicum febrile Magnan’s *[The alcoholic febrile delirium of Magnan]*. Centralblatt fuer Nervenheilkunde und Psychiatrie 15, 437; 5 pages
27. Alzheimer A (1905) Haben wir bei den verschiedenen Geisteskrankheiten mit anatomischem Befund einen histologisch annaehernd gleichen Krankheitsprozess vorauszusetzen? *[Do we have to postulate a histologically very similar disease process in different mental diseases with anatomical findings?]* Neurologisches Centralblatt 24, 680; 3 pages
28. Alzheimer A (1905) Progressive Paralyse und endarteriitische Hirnlues *[Progressive paralysis and endarteritic lues cerebri]*. Centralblatt fuer Nervenheilkunde 16, 443; 3 pages
29. Alzheimer A (1906) Ueber den Abbau des Nervengewebes *[On the degradation of the nervous tissue]*. Allgemeine Zeitschrift fuer

18 Referat

Psychiatrie und psychisch-gerichtliche Medizin 63, 568; 5 pages
30. Alzheimer A (1906) Ueber einen eigenartigen, schweren Erkrankungsprozess der Hirnrinde *[On a peculiar, severe disease process of the cerebral cortex]*. Neurologisches Centralblatt 25, 1134 *[reference to the lecture only, no abstract]*
31. Alzheimer A (1906) Zur pathologischen Anatomie der Paralyse und der paralyseaehnlichen Erkrankungen [On the pathological anatomy of paralysis and paralysis-like diseases]. Muenchener medizinische Wochenschrift 53, 1643; 1 page
32. Alzheimer A (1907) Ueber eine eigenartige Erkrankung der Hirnrinde *[On a peculiar disease of the cerebral cortex]*. Zeitschrift fuer Psychiatrie 64, 146; 3 pages
33. Alzheimer A (1907) Einige Methoden zur Fixierung der zelligen Elemente der Cerebrospinalfluessigkeit *[Several methods of fixation for cellular elements of the cerebrospinal fluid]*. Centralblatt fuer Nervenheilkunde und Psychiatrie 18, 449; 3 pages
34. Alzheimer A (1907) Die Gruppierung der Epilepsie *[The categorisation of epilepsy]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 64, 418; 4 pages
35. Alzheimer A (1907) Ueber die Indikationen fuer eine kuenstliche Schwangerschaftsunterbrechung bei Geisteskranken *[On indications for an induced abortion in lunatics]*. Muenchner Medizinische Wochenschrift 54, 1617; 5 pages
36. Alzheimer A (1907) Die stationaere Paralyse *[The stationary paralysis]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 64, 670 (656); 8 pages
37. Gaupp R, Alzheimer A (1907) Die Frage der stationaeren Paralyse der Irren *[The question of stationary paralysis of the lunatics]*. Centralblatt fuer Nervenheilkunde und Psychiatrie 245; 18 pages
38. Alzheimer A (1909) Die syphilitischen Geistesstoerungen *[The syphilitic mental disturbances]*. Allgemeine Zeitschrift fuer Psychiatrie und psychisch-gerichtliche Medizin 66, 920; 10 pages
39. Alzheimer A (1910) Ueber Degeneration und Regeneration an der peripheren Nervenfaser *[On degeneration and regeneration at the peripheral nerve fibre]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie Ref. 1, 654; 2 pages
40. Alzheimer A (1910) Beitraege zur Kenntniss der pathologischen Neuroglia and ihrer Beziehungen zu den Abbauvorgaengen im Nervengewebe *[Contributions on the understanding of the pathological neuroglia and their relationships to the breakdown processes in nervous tissue]*. (Nissl's-Alzheimer's) Histologische und Histopathologische Arbeiten. Band 3, 401; 162 pages and 8 plates with illustrations
41. Alzheimer A (1910) Die diagnostischen Schwierigkeiten in der Psychiatrie *[The diagnostic difficulties in psychiatry]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 1, 1
42. Alzheimer A (1911) Ueber die anatomische Grundlage der Huntingtonschen Chorea und der choreatischen Bewegungen ueberhaupt *[On the anatomical basis of Huntington's chorea and the choreatic movements in general]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 3, 566; 2 pages
43. Alzheimer A (1911) Ist die Einrichtung einer psychiatrischen Abteilung im Reichsgesundheitsamt erstrebenswert? *[Is the establishment of a psychiatric department at the central ("Reichs") health authority desirable?]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 6, 242; 5 pages
44. Alzheimer A (1911) Ueber eigenartige Krankheitsfaelle des spaeteren Alters *[On peculiar cases of disease at higher age]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 4, 356; 30 pages and 2 plates with illustrations
45. von Hoesslin C, Alzheimer A (1912) Ein Beitrag zur Klinik und pathologischen Anatomie der Westphal-Struempellschen Pseudosklerose *[A contribution on the clinical features and the pathological anatomy of the pseudosclerosis Westphal-Struempell]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 8, 183; 27 pages and 1 plate with illustrations
46. Alzheimer A (1912) Ergebnisse auf dem Gebiete der pathologischen Histologie der Geistesstoerungen *[Results in the field of the pathological histology of mental distur-bances]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 5, 753; 28 pages
47. Alzheimer A (1912) Die Bedeutung der Symptomenkomplexe in der Psychiatrie, besonders im Hinblick auf das manisch-depressive Irresein *[The importance of symptom complexes in psychiatry, especially with respect to manic-depressive disease]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie Ref. 5, 806; 5 pages
48. Alzheimer A (1913) Ueber noch nicht genauer bekannte paralyseaehnliche Krankheitsbilder *[On paralysis-like disorders that are not yet known in detail]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie Ref. 6, 1074; 2 pages
49. Alzheimer A (1913) 25 Jahre Psychiatrie. Ein Rueckblick anlaesslich des 25jaehrigen Jubilaeums von Prof. Dr. Emil Sioli als Direktor der Frankfurter Irrenanstalt *[25 years in psychiatry.* A look back on the occasion of the 25th anniversary of Prof. Dr. Emil Sioli's directorship of the Frankfurt mental asylum]. Archiv fuer Psychiatrie und Nervenkrankheiter

52, 853; 14 pages
50. Alzheimer A (1913) Ueber die Abbauvorgaenge im Nervensystem *[On the degradation processes in the nervous system]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie Ref. 8, 81; 2 pages
51. Alzheimer A (1913) Beitraege zur pathologischen Anatomie der Dementia praecox *[Contributions on the pathological anatomy of the dementia praecox]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie, Ref. 7, 621; 2 pages
52. Alzheimer A (1913) Ueber zwei verschiedene Typen von Entwicklungshemmungen des Gehirns *[On two types of developmental malformations of the brain]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie, Ref. 8, 289; 2 pages
53. Alzheimer A (1914) Ueber einen Fall von Poliomyelitis bulbi et cerebelli *[On a case of poliomyelitis bulbi et cerebelli]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie, Ref. 8, 534; 1 page
54. Alzheimer A (1914) Ueber einen Fall von „hysterischer Bulbaerparalyse“ *[On a case of „hysterical bulbar palsy“]*. Zeitschrift fuer die gesamte Neurologie und Psychiatrie, Ref. 8, 534; 2 pages
55. Alzheimer A (1914) Ueber den gegenwaertigen Stand der Lehre von der Epilepsie *[On the current status of the teaching on epilepsy]*. Deutsche medizinische Wochenschrift 40, 1451; 1 page
56. Alzheimer A (1915) Faelle von Methylalkoholvergiftung *[Cases of methyl alcohol intoxication]*. Deutsche medizinische Wochenschrift 41, 635; 1 page
57. Alzheimer A (1916) Ueber eine eigenartige Erkrankung des zentralen Nervensystems mit bulbaeren Symptomen und schmerzhaften spastischen Krampfzustaenden der Extremitaeten [On a peculiar disease of the central nervous system with bulbar symptoms and painful spastic cramps of the extremities]. Zeitschrift fuer die gesamte Neurologie und Psychiatrie 33, 45; 15 pages and 1 page with illustrations *[posthumous, edited by W. Spielmeyer]*