- 4 Blevins G, Macaulay R, Harder S, et al. Oculoleptomeningeal amyloidosis in a large kindred with a new transthyretin variant Tyr69His. Neurology 2003:**60**:1625–30.
- 5 Herrick MK, DeBruyne K, Horoupian DS, et al. Massive leptomeningeal amyloidosis associated with a Val30Met transhyretin gene. *Neurology* 1996;47:988–92.
  Mitsuhashi S, Yazaki M, Tokuda T, *et al.* MRI analysis on a patient with the V30M
- mutation is characteristic of leptomeningeal amyloid. Amyloid 2004;11:265-7
- 7 Munar-Ques M, Salva-Ladaria L, Mulet-Perera P, et al. Vitreous amyloidosis after liver transplantation in patients with familial amyloid polyneuropathy: ocular synthesis of mutant transthyretin. *Amyloid* 2000;**7**:266–9
- Schreiber G, Aldred AR, Jaworowski A, et al. Thyroxine transport from blood to brain via transthyretin synthesis in choroid plexus. Am J Physiol 1990;258(Pt 2):R338-45.

## HISTORICAL NOTE

- 9 Dickson PW, Schreiber G. High levels of messenger RNA for transthyretin
- (prealbumin) in human choroid plexus. Neurosci Lett 1986;**66**:311–15
- Stangou AJ, Hawkins PN. Liver transplantation in transthyretin-related familial amyloid polyneuropathy. Curr Opin Neurol 2004;17:615–20. Adams D, Samuel D, Goulon-Goeau C, et al. The course and prognostic factors of familial amyloid polyneuropathy after liver transplantation. Brain
- 2000;**123**:1495-504.
- 12 Ando Y, Terazaki H, Nakamura M, et al. A different amyloid formation mechanism: de novo oculoleptomeningeal amyloid deposits after liver transplantation. *Transplantation* 2004;**77**:345–9.
- 13 Ellie E, Camou F, Vital A, et al. Recurrent subarachnoid hemorrhage associated with a new transthyretin variant (Gly53Glu). Neurology 2001.57.135-7

doi: 10.1136/jnnp.2006.106633

## Johann Bernhard Aloys von Gudden: an outstanding scientist

ohann Bernhard Aloys von Gudden was a visionary psychiatrist and neuroanatomist. He dedicated himself to I neurobiology and was far more than a consulting psychiatrist to the Bavarian royal family. Some well-known scientists such as Emil Kraepelin (1856–1926), Franz Nissl (1860–1919), Auguste-Henri Forel (1848-1931) and Sigbert Josef Maria Ganser (1853-1931) studied under his supervision.

von Gudden was born in Kleve, in lower Rhineland near the Dutch frontier. on 7 June 1824. He was the third of seven sons of Johannes Gudden, a landed proprietor, owner of a brewery and member of the town council. In 1843, he began his studies in philosophy and medicine at the university in Bonn. For his doctoral dissertation, von Gudden studied torsional eye movement under the supervision of Alfred Volkman (1800-77) at Halle. He received his medical degree in 1848 and in the same year passed with distinction the state medical examination in Berlin. Thereafter, he obtained a position at the Siegburg asylum as an assistant under the supervision of Karl Wigand Maximilian Jacobi (1775-1858), one of the leading German psychiatrists.

After completing his studies in Berlin in 1849, von Gudden served in the army for a year. From 1851 to 1855, he worked with Christian Friedrich Wilhelm Roller (1802-78) in the Illenau asylum near Achern, the first modern psychiatric hospital in Germany. He married Roller's granddaughter Clarissa Voigt in 1855, and, in the summer of the same year at the age of 31, was appointed the director of Werneck, a newly established asylum in northern Bavaria. In October 1869, von Gudden became director of the newly founded Burghölzli psychiatric hospital in Zürich, Switzerland, and in 1870, was appointed co-editor of Archiv für Psychiatry und Nervenkrankheiten. In 1872, he took over the direction of the Oberbayerische Kreis-Irrenanstalt in Munich, and subsequently became a full professor of psychiatry at the University of Munich.

At the height of his career, von Gudden was commissioned to provide psychiatric care for the Bavarian royal family. He was the personal doctor of the mentally diseased Crown Prince Rudolf Otto (1848–1916) for many years. He took responsibility for the everyday care of the crown prince, who was secluded in Furstenried, a castle near Munich, and subsequently was assigned to examine and treat King Ludwig II of Bavaria (1845-86). On 13 July, 2 days after King Ludwig II was arrested at Castle Neuschwanstein, Ludwig II and Bernhard von Gudden drowned in Starnberg Lake, close to the castle of Berg. The details surrounding their death remain unclear. For some incomprehensible reason, no autopsy was ever performed on von Gudden to determine the cause of death.

In the last 14 years of his life, von Gudden devoted himself to the study of neuroanatomy, a rapidly developing science in the 19th century. He was the first neuroanatomist to create lesions in the nervous system of newborn animals and to study the subsequent anatomical changes. In this work, he applied the

technique of secondary degeneration to study important interrelationships between the cortical and subcortical structures. Today, this method, based on retrograde neuronal cell body changes observed after nervous system lesions, is still referred to as the von Gudden method. A published article<sup>1</sup> shows that he was clearly aware of the limitations of this method; he was not so much interested in the description of brain centres, but was concerned with the independencies and connections between the centres.

Macroscopic observation was widely used in von Gudden's time, as microscopy was still unsatisfactory. Therefore, he pioneered the development of a microtome, the so-called Gudden's microtome,<sup>2</sup> for sectioning the human brain, and using this he described the important neuroanatomical centres. His assistant, Auguste-Henri Forel, subsequently improved the microtome, and thus he was able to obtain entire human brain sections, at about 55 µm in thickness.

von Gudden is perhaps best known for his studies on partial decussation of the optic paths, a subject that kept him occupied for around 30 years. His method of producing secondary atrophy of central structures after the removal of sense organs or cranial nerves in young animals ushered in a fresh advance in experimental neurology. In fully grown animals, from which eyes had been removed when they were young, he showed not only crossed and uncrossed optic fibres but also a supraoptic commissure and the transverse peduncular tract. Both of these tracts now bear his name. He was the first to describe the interpeduncular nucleus and the tegmental nuclei, known to all who work in the midbrain today as the dorsal and ventral nuclei, respectively, of Gudden.

One of Gudden's greatest contributions was his observation in 1870 that destruction of certain areas of the cerebral cortex leads to atrophy of specific thalamic nuclei. Augustus Volney Waller believed that, after a cut, the cell body and central stump of the nerve remained normal, but Gudden found that they showed signs of atrophy. Accordingly, he launched a series of investigations in which he used his "secondary degeneration technique"-that is, the Gudden method-to trace connections between the main centres of the brain.

## Levent Sarikcioglu

Correspondence to: Dr L Sarikcioglu, Department of Anatomy, Akdeniz University, Faculty of Medicine Campus, Antalya 07070, Turkey; sarikcioglu@akdeniz.edu.tr

## References

- von Gudden JBA. Experimentaluntersuchungen bei das peripherischer und centrale Nervensystem. Arch Psychiatr Nervenkr 1870;2:693-723.
- 2 von Gudden B. Über ein neues microtom. Arch Psychiatr Nervenkr 1875:5:229-34