Otto Friedrich Karl Deiters (1834–1863)

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ABSTRACT

Otto Deiters, for whom the lateral vestibular nucleus and the supporting cells of the outer auditory hair cells were named, died in 1863 aged 29. He taught in the Bonn Anatomy Department, had an appointment in the University Clinic, and ran a small private practice. He published articles on the cell theory, the structure and development of muscle fibers, the inner ear, leukaemia, and scarlet fever. He was the second of five surviving children in an academic family whose private correspondence revealed him to be a young man with limited social skills and high ambitions to complete a deeply original study of the brainstem and spinal cord. However, first his father and then his younger brother died, leaving him and his older brother responsible for a suddenly impecunious family as he failed to gain academic promotion. Otto died of typhus two years after his younger brother's death, leaving his greatest scientific achievement to be published posthumously. He showed that most nerve cells have a single axon and several dendrites; he recognized the possibility that nerve cells might be functionally polarized and produced the first illustrations of synaptic inputs to dendrites from what he termed a second system of nerve fibers. J. Comp. Neurol. 521:1929–1953, 2013.

INDEXING TERMS: history; Deiters cells; Deiters nucleus; axons; dendrites; synapses

Otto Deiters died on December 5, 1863, 150 years ago. When he died, he was 29, unmarried, and had been working intensely on what might have become an early textbook of neuroanatomy and neurohistology. He had been working under adverse conditions; he had a recently widowed mother and two teenage sisters in need of financial support, and his younger brother had died shortly after his father's death. His efforts to establish a career as a neuroanatomist at Bonn University, with the strong support of his professor, Max Schultze, had been unsuccessful in spite of his significant published scholarly contributions. The unpublished material he left behind reveals a microscopist and illustrator of unusual skill with deep insights into the problems that faced our predecessors. It is difficult not to speculate what he might have achieved had he lived into the 20th century, as did his older brother, Hermann.[1]

In this review of his life and accomplishments, the first three sections describe his personal life and the later sections his published results. We present an account of a somewhat lost young man moving from medical school to a year in Berlin, where he is greatly stimulated by the great men at the recently opened Charité (Fig. 1). He returns home and during the last few years of his short life turns himself into a gifted neuroanatomist, struggling to understand the puzzles of the brain while his family faces serious problems and his personal life is neglected.

The present authors, both descendants of Hermann Deiters (Fig. 2), met recently[2] through their shared interest in Otto's life and work. Both had wanted to learn more when, as medical students, they encountered the family name linked to the lateral vestibular nucleus and the supporting cells of the inner ear. VSD has written a

[1]He was 17 years younger than Kölliker, 18 years older than Ramón y Cajal, and 9 years older than Golgi.

[2]RWG has written, "Our acquaintance grew out of a conversation with a medical student in Istanbul, where I was teaching. The student said that a visiting German Erasmus student wanted to meet me. The German student was from Bonn. I spoke of my interest in Bonn as a place where early publications by Otto Deiters might be available and mentioned my relationship to Otto. The German student had to leave unexpectedly and I never learnt his name. Later, a medical historian at Bonn, PD Dr. Walter Bruchhausen, wrote to me, saying that a doctor at Bonn had recently written a thesis on Otto Deiters. He added that she was also called Deiters, was related to Otto, and must also be related to me. He added her address. This footnote is written as a formal thanks to Dr. Bruchhausen and the anonymous student for putting the two authors in touch, thus generating this article."

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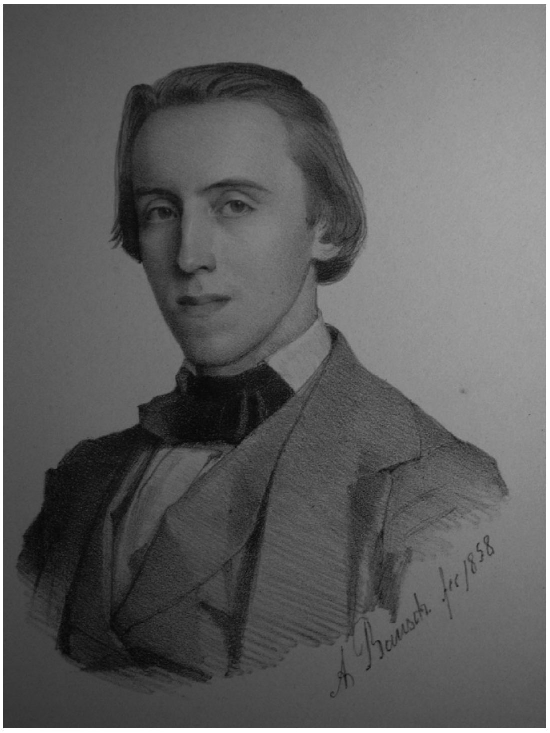

Figure 1. Portrait of Otto Deiters by August Bausch, 1858.

doctoral thesis (Deiters, 2006) based largely on personal records kept in her family, and RWG wrote briefly about Otto's work and life in three earlier papers. One marked the 100th anniversary of Otto's death (Deiters and Guillery, 1964) and was written with his great aunt, who was a psychiatrist in Düsseldorf and the daughter of Otto's Brother Hermann. The other two were about the neuron doctrine that included comments on the relevance of Otto's work (Guillery, 2005, 2007). We combine and extend these earlier studies now to mark the 150th anniversary of Otto's death. He died showing significant promise of becoming one of the great neurohistologists of his generation. Most of the material presented in the early sections is based on VSD's thesis, and the rest is largely based on Otto's published work.

EARLY LIFE AND EDUCATION

Childhood

Otto Deiters was born on November 15, 1834, the second son of Franz Peter Ignaz Deiters and Emilie Eleonore Henriette Deiters (born Bausch). The family tree in Figure 2 includes his siblings, two of which died in their infancy; Otto and his younger brother Max died before they were 30. The father was a professor in the Law Faculty of Bonn University. He served five terms as Dean of the Faculty and two (1845–1846 and 1856–1857) as Rector. The University, founded in 1818 and small by today's standards, had many eminent faculty members including von Helmholtz, Johannes Müller, and Eduard Pflüger, and students including Theodor Schwann (who followed Müller to Berlin), Heinrich Heine, Prince Albert, and Karl Marx. Bonn was a small town of 35,000[3] inhabitants, first reached by the railway in 1848. In that year Franz Peter Deiters served as an elected representative from Bonn to the Frankfurt National Assembly, which attempted to establish a parliamentary democracy in Germany.[4] He served on the constitutional committee of that parliament as a liberal member. He died, aged 57, in 1861, leaving a financially strapped widow and five children still needing financial support: Hermann just 27, Otto at 26 struggling to establish his professional status, a younger brother Max, at 23 starting a career in mining, and the two youngest daughters, aged 15 and 19.[5]

The family was, like most others in the Rhineland, Catholic. It was a respectable and serious academic family, the children learning Latin and French at an early age.[6] When he was 10, Otto wrote in German to his parents: "Today on the first day of the New Year, I find myself particularly impelled (besonders angetrieben) to say to you in writing, how much I love you and my heart thanks you for the manifest blessings (erzeigten Wohltaten). May the Almighty hear my prayer and grant you the proper blessings, for your great care and the many sacrifices you have made to give me pleasure and through a good upbringing make me happy...."[7] This was a family dedicated to high academic achievement.

While the father was at the Frankfurt parliament, he wrote to 15-year-old Hermann about some political issues Hermann had raised, advising him not to get involved with politics as they might keep him from his present duties (presumably school), and then adding that he would like to hear more about what he and Otto did during the holidays, "...and at your next opportunity to communicate this also to Otto. If it is not overly burdensome for Otto, with a definite topic in mind letter writing would not be as difficult as he

[3]https://commons.wikimedia.org/wiki/File:Bonn_population.svg. This compares to Berlin's 400,000 at the same time (Namier, 1992).

[4]This "revolutionary" parliament included 49 university professors and lecturers and 57 schoolmasters among its more than 800 elected members, according to Namier (1992), who described the 1848 revolution as the revolution of the intellectuals.

[5]We have no information about the reasons for the family's financial problems. They added to the pressures on Otto before his own death two and a half years after his father's and two years after that of his younger brother, Max.

[6]Hermann wrote accounts of his holidays in Latin for his father.

[7]Quotation marks here and subsequently show passages translated from the German. Parentheses enclose original German words having possible alternative meanings.

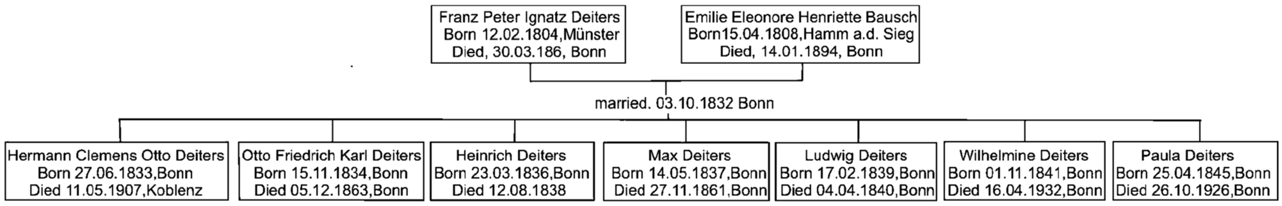

Figure 2. Family tree of the immediate Deiters family.

seems to believe. This would please me especially, although you can assure Otto that I have not taken his past silence amiss, but have understood it." The father was aware of Otto's withdrawn and unsociable nature, which figures significantly in the family correspondence, and one wonders how much of the father's message Hermann passed on to Otto.

The family was musical. Otto played violin and viola. He and Hermann organized a musical circle in 1852 that met every week and played classical music, mostly quartets, whose rules still survive (Deiters, 2006). The last rule states that each member has the duty to practice with others and if necessary on their own. Hermann was much more sociable and outgoing than Otto and had a lifelong interest in music; much of the correspondence between the brothers was about music or drama, complete with details of performances and critical comments, e.g., "Mr. Frank from Cologne played Beethoven's C minor piano concerto, then a Bach fugue, which I have never heard you play, and then a little charming composition of his own...and then Frau Nissen Salomon sang a few charming Swedish songs and a quite abominable aria by Verdi tolerably, but a wonderful aria from Alessandro Stradella very badly. She trilled and warbled frightfully."[8] This group of musicians continued to meet while Otto was in medical school and included a fellow medical student, Carl Liebermeister (see below).

Medical school at Bonn (1852–1857)

In 1852 Otto graduated from his school with positive comments from his teachers about his moral leadership, his diligence and his knowledge of the subjects that included, German, Latin, Greek, French, Hebrew, Religious studies, Mathematics, History and Geography, Physics and Philosophical Propaedeutics. He started in medical school with no Biology or Chemistry, which would play a major role in his later studies. Although his father and older brother studied humanities, he was not the only medical student in the family. A maternal uncle, Friedrich Bausch, had studied medicine at Bonn in 1832 and left a bound 400 page volume of his neatly handwritten notes of the lectures that Johannes Mueller delivered to the students that year[9].

In reaction to Hermann's suggestion, that Otto was not establishing enough friendships, Otto wrote: "You seem to think that I am one of those who invest all of their needed learning abilities in the courses and who have a who knows what sort of a conscience if they just once, horribile dictum, cut classes for an hour. There you are mightily in error... as a medic one is closer to the professors, and if in addition to that one is the son of one's father and the father happens to be a colleague of the professor, if, further, one is sitting with a maximum of 3 to 6 colleagues, then you will understand that one can't always do what one wants."

We have relatively little information about Otto's years in medical school. As the above letter shows, he felt isolated. His later correspondence (see the next section) indicates that he still had to learn to focus his studies on the essentials. His musical activities continued, but he worked through his studies rather mechanically, and he wrote to Hermann in 1854: "I go to the college, then sit again in my room, go again to the college and then sit once more in my room, and that's how it goes, from one day to the next. There are no people that I am close to, I have no friends. That's bleak (trostlos), isn't it?" We have very little information about this period of his life. He was living at home, was insecure about his studies, and left limited correspondence.

Otto's doctoral thesis, "De Incremento Musculorum" (Deiters, 1856), in Latin, was about the growth of muscles, documenting the sizes of many different muscles in many different species (human, ox, rabbit, dormouse, dove, several species of frog, salamander and carp), comparing ages, and on the basis of the means and what would today be recorded as variances of the measurements concludes that muscle growth is due to an increase of the volume of the individual muscle fibers not to an increase in their numbers[10]. His thesis advisor was Julius Budge.

[8] A letter from Otto to Hermann, November 17, 1854.

[9] Now held by Bonn University.

[10] For non-Latin speakers Otto summarizes this study in Deiters (1861a), with regrets that these results are not well known.

BERLIN: LIVING AWAY FROM HOME, MILITARY DUTY, AND LECTURES AT THE CHARITÉ (1857–1858)

Otto's one year in Berlin was an important period in his short life, significantly igniting his interest in medical studies. Although this was primarily his year as a volunteer in the army, it included attendance at lectures by Virchow, Johannes Müller, and Romberg, and was the only extended period of his life away from his family. It stimulated him to start thinking seriously about his career goals, and woke him to a wider view for his future. Otto served as a volunteer in the artillery of the 2nd Guards Regiment in Berlin. He had a low view of the military and for him this was primarily an opportunity to visit Berlin and attend Virchow's lectures at the recently established Charité. Writing to his younger brother Max, he evaluated his choices, basing them on how close to the University the barracks were, how well educated the officers were, and the severity of the drill exercises. Of the artillery he wrote: "...when the regiment is on the move the soldiers dawdle without a heavy pack and in no strict order behind the cannon," contrasting this to the soldiers of the infantry with heavy packs and in strict order.[11]

Otto went to Berlin two months ahead of his army service so he could attend Virchow's lectures. Virchow had written: "Only a few have advanced enough to have learnt really to think in microscopical terms.... For most older doctors, microscopy is like a foreign language, where one can freely use foreign words but thinks in one's own language."[12] Otto's brief period with the students who were learning the "new language" from Virchow would be strongly reinforced after his return to Bonn in 1858 by Max Schultze, who was appointed to the Bonn Anatomy chair in 1859. Virchow had also written: "The natural scientist knows the body and the properties of the body, what is beyond he calls transcendent and regards the transcendent as an error of the human mind." Otto cited this at the head of his dissertation.

During this period in Berlin, Otto also attended the comparative anatomy lectures of Johannes Müller, and wrote to Hermann, "...everything that M says is significant and ingenious to the highest degree but in one summer semester there is not time to go into the special points, and this also applies to Virchow's pathological anatomy. In both [fields] private studies are essential. Here microscopic anatomy is only taught by younger staff (Privatdocenten). For my own studies one thing is absolutely necessary. Requirement one microscope."[13]

The father had previously advised Otto to borrow a microscope, and Otto had told him this was impossible. The crucial issue at the time was the achromatic lens, which was produced by only a few companies, and provided much clearer views because these lenses corrected the chromatic aberration characteristic of earlier lenses, which had brought each wavelength to a different focal point and introduced significant blurring of the image, especially at higher magnifications. In July 1857 the father advised Otto that Leitz had begun to produce microscopes that were greatly in demand and told Otto not to delay in placing his order. It appears that the father found funds, but did not live long enough to see the extraordinary results Otto would produce.

Here we encounter the sad financial position of the Deiters family. Otto's father had previously written to a colleague requesting help to find a position for Otto, his talented but impecunious son. The father complained about his own financial position, and added "if you find him [Otto] somewhat enclosed, restrained, reserved (verschwiegen), then I can tell you that I hear and have grounds for believing that if this ring can be broken, a good core will be found" (Deiters, 2006). Not surprisingly, the letter produced nothing.

The letters from Otto in Berlin to his brothers (cited more fully in Deiters, 2006) are entertaining and include critiques of (good and bad) musical performances in Berlin, showing that he was more aware of others than many of his later actions and his views of himself might suggest. He writes about the Tiergarten, implicitly comparing city promenades with the real walks possible in the Rhineland. The Tiergarten walks are spoilt by the many typical Berliner family outings: "...maids with their cousins and children, old women in Amazon hats (Grisetten in Amazonhüten),[14] careful parents with their marriageable daughters...arrive at one of the many inns, they all sit, the whole Berliner hoi-polloi (Philisterium), each family at one table in the middle of which a towering glass of Weissbier (eine Weisse) is enthroned, and then with dignified demeanour the honoured family father takes a draught whereupon the others follow in order (secundum ordinensis). Such a thing is only possible in Berlin...."

[11]Otto to Max Deiters, May 18, 1858. This was before the reorganization of the Prussian Army (see Grenville, 1976).

[12]Cited by Deiters (2006).

[13]Otto to Hermann, May 26, 1857.

[14]A stylish hat. A poem appeared in 1857 entitled " Der Amazonenhut–Mit achtzehn Jahren wohlgetan–mit zweiundzwanzig geht's noch an–Mit dreißig Jahr' bewahr' uns Gott!–Mit sechsunddreißig–Kinderspott!" See "Eisenbergisches Nachrichtsblatt 1857 at http://zs.thulb.uni-jena.de/receive/jportal_jparticle_00081264. In English: The Amazon hat: At 18 it is well done–at 22 just possible–at 30, 'God preserve us'–and at 36 the children mock.

Otto's Berlin letters also tell us more about family relationships: "Papa's letter has arrived safely. The somewhat unworthy (unwürdige) title, junior doctor, can be left out of the address." Another letter, in which Otto replies to Hermann's request that Otto look in Berlin for a suitable silver wedding gift for the parents, provides a close domestic view: "We must respect the principle of usefulness so valued in our home." Such items as pictures or valuable rings are not to be considered. He discusses a clock for the hall or some comfortable chairs, which may be needed, but advises that they can be purchased in Bonn or Cologne as well as Berlin. We do not know whether the family gained the comfortable armchairs they lacked or the clock that would keep them all on time.

In 1857 Otto also began to act as informal medical adviser to Hermann, sounding authoritative, dogmatic, and uncompromising. On the basis of Hermann's account of his indisposition, Otto had diagnosed a gastric and intestinal problem, "perhaps augmented, so far as I can see, by a gallbladder problem. . .you think that in spite of Albers's[15] energetic treatment you are not completely cured. I can believe that. These conditions usually go away on their own without any energetic treatment. . .above all you must not be thinking about yourself as having an unhealthy nature. Our family has a healthy nature." Otto goes on to advise Hermann to live a less sedentary life, take more walks, exercise, and drink less tea and coffee. He sounds stern, not like a younger brother. Hermann must have replied by reporting that he was better, and complaining that he was not ready to follow Otto's rather rigorous rules, because Otto's next letter expresses pleasure at the improvement and hopes it will last: "You consider the correct dietary regime to be of no consequence, and I could hardly expect anything different, but that must not be. . .." Another harangue about healthy diet and exercise follows complete with a statement about patients who fail to follow the doctor's advice. But he ends on a peace-making note, saying, "I did not mean, as you seem to have assumed. . .that you should at this point give up your social life and follow my bad example."

Although Otto was a private, self-enclosed person and was recognized as such by family and colleagues, he had some close friends, including his fellow musicians, particularly Carl Liebermeister,[16] with whom he corresponded after they graduated. The letters from Liebermeister contain advice about examiners at other universities. From Greifswald, where he was studying, he wrote: ". . .he who knows his subject reasonably well is better off going to Greifswald, but he who knows nothing could fake his way in Berlin. . ..You could, with a clear conscience, advise people to go to Greifswald." He invited Otto to visit him in Greifswald, and a later letter to Otto from N. Simrock, school friend and fellow medical student, includes a statement that he was glad to hear that the two had met: "You both always followed the same academic tendencies." Later, Otto visited Tübingen while Liebermeister was there as prosector in Pathological Anatomy.

While he was in Berlin, Otto began to think seriously about his future. He wrote a thoughtful letter to Hermann: "I have always worked hard, though not as hard as people said. I had to, because quite apart from the amount of material that had to be mastered, which was overpowering, the time that was available to me because of my reserved nature had to be occupied. There was a lack of distractions. So at the beginning this work was not of the right sort." He now sees more specialist areas that he had no time to review properly as a student. "I don't think that I judge my strengths too highly but I don't want to estimate them too lowly. . .. The position at present is as follows: I no longer doubt that I would prefer an academic career to one in a practice. . .this fits best with my strengths. So I will be a docent, no matter what." He then asks about the long-term possibilities of an academic career and about his choices. He is clear about these: on the one hand, anatomy, particularly microscopic and comparative anatomy, and on the other, pathological anatomy. He considers an assistant position with Geheimrat Naumann in Bonn as a docent in pathological anatomy, and finding a medical practice that would later provide extra income (Später die nöthigen Bedürfnisse deckte). However, he worries about income, and sees a Professor of Pathological Anatomy as a "fifth wheel," not making much money, while a serious clinical commitment would limit his plans for academic work. He reflects negatively about the position of a doctor in a German practice: "If I don't settle in the first best village and don't go to America, then I would risk as little by planning on a simple academic career as I would by expecting a remunerative practice: particularly so as the field to which I always return has many income possibilities. And that field. . .is anatomy. . .and I have decided to dedicate myself to it." He lists the income opportunities: publications generated income then, as did private tutorials, which were more in demand as exams increased in difficulty.

He decided nonetheless to maintain his clinical skills, and in Berlin attended the clinical sessions presented by Romberg and Langenbeck.

[15]Another Bonn faculty member in the pathology department.

[16]Later Professor of Pathology and Therapy in Basel from 1865 and in Tübingen from 1871 (Deiters, 2006).

N. Simrock, who had moved to Cologne, compared Otto's enthusiasm about academic opportunities with his own lack of academic ambition. He was glad to be in Cologne, he wrote, where "...a zealous academic engagement is impossible...I know for you it is different, and even if your well-known unassuming modesty stops you from recognizing it, it will later be a benefit for the faculty that has the good luck to count you among its young chosen ones."

In another letter, before Otto moved back to Bonn, Simrock wrote about Otto's planned appointment with Naumann: "That you have accepted the position with Naumann not only does not surprise me, but, on the contrary, I think it totally understandable, since in such a position you can soonest reach your goals. Only I would...in relation to him put myself in an independent position, which is something he may assume." Here Simrock anticipates later problems for Otto's career, based on the differing approaches to medicine of Otto and Naumann: the former scientific, the latter philosophical and romantic.

In 1858 Otto completed his military service and returned to Bonn as first assistant to Geheimrat Naumann, spending the next three years with him.

MEDICAL CAREER IN BONN (1858–1863)

Clinical work and publications

In Bonn Otto took on clinical responsibilities in Naumann's clinic and also started private clinical work as a general practitioner, visiting patients in Bonn and surrounding areas[17] to boost his income. He also began to work on his habilitation, which would qualify him as a lecturer at the University. He must also at an early stage have begun detailed investigations of the inner ear in several different species, which led to four publications by 1862 (see the section, The organ of Corti and Deiters cells, below).

In 1859 he published a brief account of two cases of scarlet fever (Deiters, 1859a) and later a longer article about leukemia (Deiters, 1861a). The former stressed that current treatments were generally ineffective and showed that incidence of the infection could not be related to particular home conditions of the patients; the latter presented a detailed account of the physical (wasted) condition of a terminally ill young man who died in the hospital. Otto described the postmortem findings, the major features being lymphatic swelling of the peritoneum, in which he noted hypertrophic cells and abnormal blood cells. He stressed how little was known about the disease. From our point of view, his rigorous demand for convincing evidence before coming to any conclusions about a disease is the most noteworthy part of both accounts.

Habilitation

Otto wrote an essay on the present position of the cell theory (Deiters, 1859b). It has a strange beginning: "Half a century has passed since the sharp eyes of a genial French investigator succeeded in winning an insight for academic anatomy that until then was completely strange and for which hardly anyone else was suited...." The long, complex sentence continues, but Xavier Bichat, who is often regarded as the father of histology (although he never used a microscope), is not identified as the sharp-eyed French investigator until Deiters had introduced many others (Leeuwenhoek, Malpighi, Linnaeus, and Cuvier) and compared their efforts at categorizations in biology with the successes of chemists, Lavoisier in particular. In this long, "scholarly" review, Otto covered much of the relevant literature, although the version that was published as a lecture lacked a list of references and looks as though it was prepared in a hurry, probably because Otto needed the qualification to start giving lectures that would bring in some fees. Although it is now considered that the cell theory was established earlier by Schleiden and Schwann, when Otto wrote, there was significant disagreement about exactly what the cell theory claimed and how far Schwann's account was an acceptable view of how tissues are organized and develop (for fuller historical accounts, see Baker, 1948, 1949; Harris, 1999). Otto had started to look at the inner ear and had noticed some cells that had a large hole, which had pushed the cytoplasm, nucleus, and nucleolus to a small border region. For reasons not made clear, Otto found it difficult to conceive of these fenestrated cells as bound by a membrane. He introduced these cells as presenting one of several difficulties faced by the cell theory at that time. Other difficulties included cells lacking a nucleus and cells lacking a nucleolus. The lack of a membrane long remained a difficulty until the electron microscope allowed clear identification of the thin, approximately 5-nm cell membrane.[18] Otto is looking for a strong theory based on the physics and chemistry of the cell, one that covers not only the anatomy of the cell but also the physiology. Even the strongest, most basic part of the cell theory, that cells only arise from other cells, he considers not yet sufficiently well

[17] He advised the patients on the local farms to not drink fresh milk, but his advice went largely unheeded.

[18] The 1948 edition of Maximow and Bloom's *A Textbook of Histology*, predating the use of electron microscopes in biology, relied on the semipermeable nature of the membrane and its resistant and elastic properties demonstrable by microdissection as the major evidence for the existence of a cell membrane.

established, in spite of mounting evidence, which he summarizes. The problem of exactly what the cell theory does include was not resolved at the time and may even today not be clearly agreed. This is an issue that plays an important role in Otto's later work and is revisited in the section on Otto's book, below.

EARLY PUBLICATIONS IN ANATOMY

The organ of Corti and Deiters cells

In 1859, soon after returning to Bonn, Otto published an important study of the organ of Corti (Deiters, 1859c) that included a detailed account of the cells that, at Max Schultze's suggestion, were later named Deiters cells. These cells support the outer hair cells and provide a link between these hair cells and the basilar membrane. Between 1859 and 1862, Otto also published a book (Deiters, 1860a) and two other papers on the inner ear (Deiters, 1860b, 1862). These are based partially on sectioned material, but primarily rely on preparations that were teased out under the microscope. Otto compared the structures, based on their flexibility or fragility, watching how they reacted to various chemicals serving as fixatives (dichromates, chromates, or acetic acid) or dyes (iodine, carmine). These methods were widely used by early microscopists. The practice of first fixing a piece of tissue and then embedding and sectioning it before ever looking at it developed later. The method that Otto used is relevant for all of Otto's microscopic studies. He was watching the reactions of tissues to his chemical and physical manipulations under the microscope in order to reach his conclusions about their characteristics. We know no details about the microscope or the lenses that Otto used, and have no information about the "tools" that he used (probably needles, fine pipettes, delicately shaped glass rods, perhaps even fine, hand-sharpened knives, etc.).

It is important to recognize that for this work and for his later microscopic studies of nerve and glial cells, Otto's tissues were generally in an aqueous solution as he was manipulating them. They would not have been cleared in a medium of appropriate refractive index nor would he have been able to manipulate the tissue had they been covered by a coverslip.[19] Water immersion lenses were available in the late 1850s and early 1860s,[20] but we have no information about the lenses that Otto used. It is possible that Otto did some of his fine dissections with a water immersion lens, but the difficulties of manipulating small objects in conditions where surface tension effects can make the manipulations difficult (or impossible) have to be recognized. For these studies of the inner ear (see Figs. 3 and 4) and for his later studies of neurons and glia (e.g., Plate ODU II, Fig. 10), he produced extraordinary details of very small cells, often unmatched at the time, but the special tools, methods, or skills that he used are not known to us.

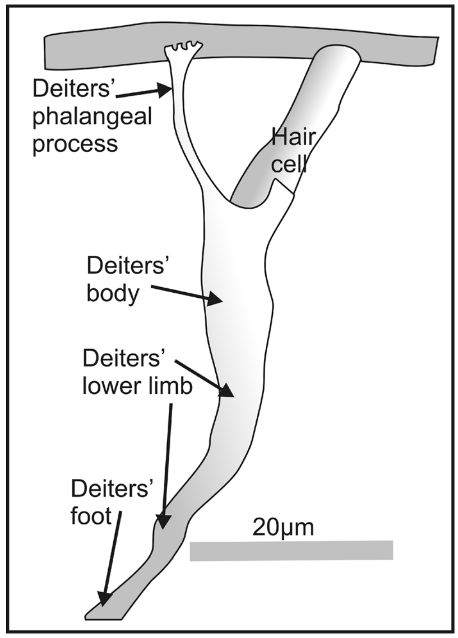

Figure 3. A Deiters cell shown schematically. The figure is based on a scanning electron micrograph (Fig. 6B of Parsa et al., 2012). The cell stretches between the reticular membrane (above) and the basilar membrane (below), and the stereocilia of the hair cells (not shown) project above the reticular membrane. Note that in the original figure there are fine nerve fibers that run horizontally across the Deiters cells. These nerve fibers are in part often enclosed within the cytoplasm of the Deiters cell and are not shown, nor are the rich terminals that lie deep within the region where the Deiters cell encloses the base of the hair cell. Scale bar = 20 μm.

Otto's first study of the organ of Corti (Deiters, 1859a) was based on material from dog, cat, and calf. It is extensively illustrated by Otto's own drawings. Otto criticizes Kölliker's earlier account of nerve fibers ending in the large "cells of Claudius," describing this as a physiological impossibility[21] but focuses on the structures that link the hair cells to the reticular lamina and the basilar membrane. Figure 3 shows the structure of a Deiters cell as seen in a current electron microscope study for comparison with Otto's figure (Fig. 4), which

[19]However, Schultze in the introduction to Otto's posthumous book mentions many microscopic preparations that Otto left behind, preserved and cleared in balsam and covered.

[20]See http://www.smecc.org/history_of_oil_immersion_lenses.htm.

[21]Presumably because the body of these nerves is in the spiral ganglion cells. Here Otto is possibly suggesting, but not exploring, an objection to a fusion of two cells. Kölliker in the 1863 edition of his textbook withdrew this suggestion on the basis of newer developmental studies but without mentioning Deiters.

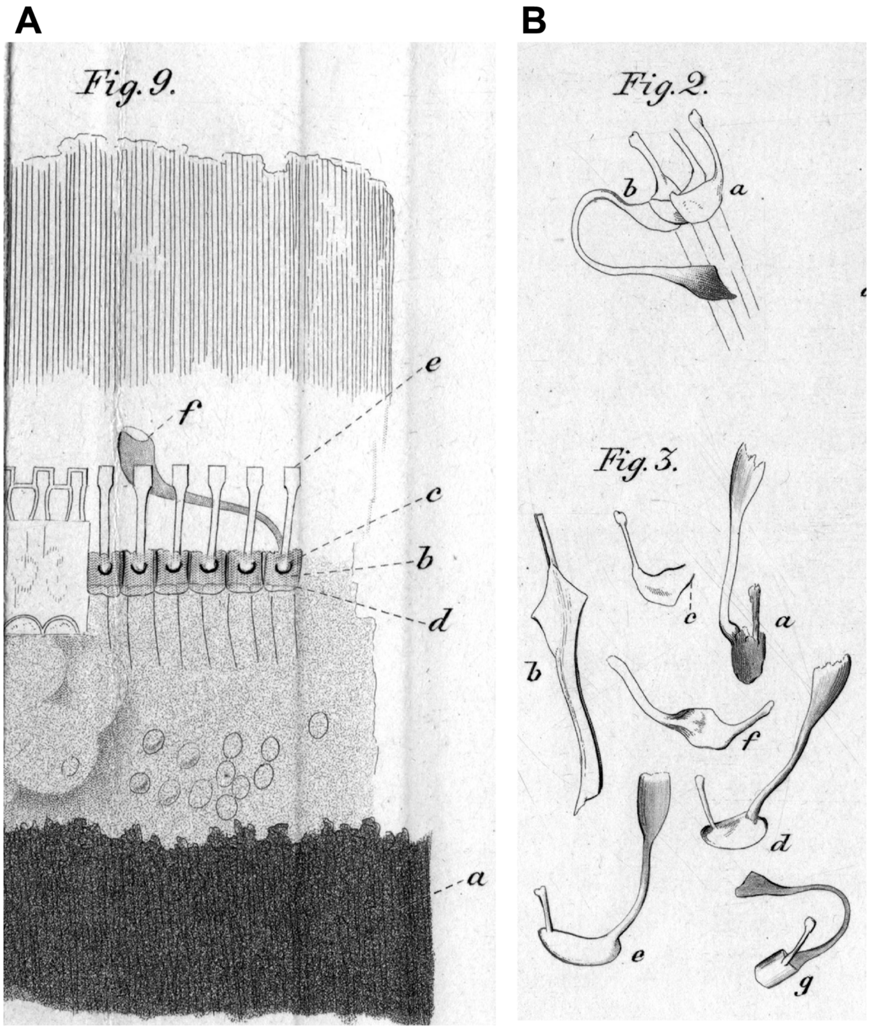

Figure 4. Otto's drawings of the cells now called Deiters cells (from Deiters, 1859c.) **A:** Figure 9 in the original publication: a, the nerve; b, the midportion of the Deiters cell; c, the region where the phalangeal process, e, joins the body of the Deiters cell (marked by a shiny circle); d, the body of the Deiters cell; f, the connection for the hair cell. (Note that d and f are left unidentified in the original). **B:** Figures 2 and 3 in the original publication. These show several views of the Deiters cells, some with the foot attached (2a, b, 3, b, f, and the others with some or all of the lower limb missing). (We thank Colin Beesley for the photographs used as Figs. 4 and 6, and for Plates ODU I–VI.)

illustrates some of the major features of the cells that now bear his name. Otto said nothing about the close relationships between these cells and the nerve fibers that are now known to be embedded in the cytoplasm of the Deiters cell as the fibers pass to the hair cells (Parsa et al., 2012). He describes the "phalangeal processes" of the cells (Figs. 3 and 4A,B), looking like tiny finger bones, extending the Deiters cells across the whole of the organ of Corti, and he shows how they relate to the hair cells in this and the later book[22] (Deiters, 1860a). He establishes the cells as separate elements, having their own nucleus, attaching to the basilar membrane and also connecting to the hair cells and to the reticular membrane. Today they are recognized as serving to transmit changes in the shape and length of the outer hair cells to the basilar membrane (Fig. 3). The changes are induced by electrical changes produced by movement of the stereocilia of the hair cells and serve to amplify the auditory signals (see Ashmore, 2008; Nam and Fettiplace, 2010 for clearly demonstrated details[23]).

The longer book on the cochlea (Deiters, 1860a), according to Otto's foreword, had to be written because a recently published article by Boettcher (1859), which

[22]This book is available on the Web with copies of the figures in which it is often impossible to identify fine details. The availability of the book on line makes librarians reluctant to find it.

[23]It is of interest that Ashmore's review opens with a brief summary of Helmholtz's work on hearing between 1862 and 1877 that was based on contemporary studies of the anatomy of the organ of Corti. (Our thanks to Donata Oertel for an emailed tutorial on the functions of the outer hair cells.)

contained "next to some correct results, a number of incomplete and mistaken results. . .made it my duty not to wait any longer with my own results."[24] The book is based on studies of rabbit, mouse, cat, dog, calf, horse, human, and guinea pig. Two further studies (Deiters, 1860b, 1862) extended his material to birds (starling, yellow hammer, hen, pigeon, crow, magpie, two species of lizard, slow-worms, grass-snakes, and probably more than one species of frog.) Reading these studies today, or Kölliker's 1863 account, and comparing them with what is now known, shows how much our knowledge has advanced and how difficult it was in the 1860s to trace nerve fibers when they lie very close to or are enclosed in the cytoplasm of the supporting cells.

Studies of striated muscles (Deiters, 1861b)[25]

This was a continuation of his thesis on muscles, using developmental studies of muscle growth in the regenerating tip of a tadpole tail. The surviving muscle fibers grow but do not contribute to the regenerated tail. New cells form from stellate or bipolar connective tissue cells, and these develop a striated fiber along one border. He draws these finely striated fibers lying next to the cells, and parts of the fibers appearing to separate from the cells, with the fibers then growing beyond the cells. He regards the striated fibers produced in this way as an *intercellular* component that is subsequently incorporated together with the cell in a common membrane, to make a new multinucleate muscle fiber. He mentions that J. Budge disagreed with Otto's conclusions and has agreed that Otto should include a discussion of their different views, which he does. Here Otto is more than usually deferential to his former thesis adviser, who later became his friend.

TEACHING, LEAVING CLINICAL WORK, AND STARTING TO STUDY THE CENTRAL NERVOUS SYSTEM

Teaching

In April 1859 Otto was granted the position of Privatdocent. In addition to continuing with his clinical responsibilities in the hospital, he worked with his private patients and started to offer lectures in the medical school (Table 1). The lectures on auscultation were a novelty in Bonn at the time. Although Otto was popular among the students, his occasional disrespectful comments about colleagues, whose approach to medicine he considered less modern and objective than his own, damaged his relationships with some faculty colleagues and would cost him dearly before long.

A family crisis; leaving clinical work

In March of 1861, the death of Otto's father following a stroke added a significant extra burden to Otto's life, as did the death of his younger brother Max, 8 months later, under circumstances that leave suicide a possibility (Deiters, 2006). This left Hermann and Otto with the sole responsibility for supporting the family, which had to move into cheaper accommodations. The youngest daughter, Paula, started training as a teacher in order to generate her own income, with Otto writing the health certificate that supported her application. At this time Otto also started to add microscopic reports for colleagues to his own earnings and time commitments.

On May 28, 1861, he wrote a letter to a professor, unidentified on the surviving draft[26] and unknown to us, calling on the goodwill the professor had often shown Otto in the past. He reported the father's death and the family's limited financial circumstances. He mentioned his present position (Assistant in the Medical Clinic and Privatdocent in Anatomy) as holding no promise for the future and leaving only limited opportunities for scientific work. If he were to continue in Bonn, he would be forced by financial considerations to sacrifice his scientific work for practical medical activities. He asked for help in finding a suitable position and recalled that in the past the professor had indicated an inclination to find a position for Otto in Heidelberg.

We have no record of any answer from Heidelberg. Otto's views about his future in Bonn represented a correct assessment of relationships there. In spite of the family's needs, in June Otto gave notice to Naumann that in view of his changed family circumstances he would be leaving his Clinical Assistant position in the summer in order to concentrate on research. We do not know the reasons for this decision, but subsequent events suggest that he knew his microscopic studies were promising a rich harvest and that he had to concentrate on them. Otto and his chief had different approaches to medicine—modern and empirical versus older and more intuitive. The two did not relate well, as anticipated in Simrock's earlier letter. Otto

[24]Boettcher's angry reaction (Boettcher, 1860) and Otto's four-page response (Deiters, 1860c) will not be explored here, but they represent the reactions that Otto's lack of tact could generate. We have not been able to address issues of priorities that arise from this interchange.

[25]In the same year Max Schultze (1961) published a paper on muscle, arguing that each nucleus of the multinucleate muscle cell represents a distinct cell not separated from the other nuclei (cells) by any membrane. Schultze's account would have caused Otto some further problems had he lived, and should be seen in relation to Otto's interpretation in this study.

[26]Possibly Helmholtz, who had been a faculty colleague of Otto's father until 1858, and who was in Heidelberg in 1861.

TABLE 1.
Details of Lectures Delivered by Otto Deiters, 1859–1862* (Numbers on the right indicate attendance)

Summer ’59	Microscopic anatomy of sense organs (revision)	11
Winter ’59-60	Microscopic anatomy (revision)	6
Summer ’60	Microscopic anatomy of the sense organs	21
	Pathological anatomy. Announced but withdrawn before registration due to demands on available time.	
Winter ’60-61	Microscopic anatomy	7
	Course in physical/chemical diagnosis	8
Summer ’61	Selected chapters of pathological histology (not delivered)	
	Physical diagnosis	9
Winter ’61-’62	About neoplasms	5
	Auscultation and percussion	0.6
	Microscopic anatomy, announced but not given.	

*Numbers on the right indicate attendance.

received a brief response from Naumann asking him to continue until September, allowing time for a replacement. In reply, on June 21, Otto, clearly offended by this brief note, wrote a formal reply: A verbal discussion of his motives for leaving was no longer desirable: “I have had to conclude from your note that you, from your position, find my leaving not only understandable but desirable.” He writes about leaving his position under conditions of demonstrable mistrust (entschiedenen Mistrauensbeweisen), a position that should not have affected his scientific studies at all, to which he has probably given more time and effort than most of his predecessors and probably more than he, with a view to his main (professional) aims, could spare and more than he should have demanded of his own health. It is a bitter and tactless letter that ends with an offer to continue until the end of August, and “. . .in recognition of what I have achieved in addition to the strict duties for the clinic, not the least difficulties should be raised for this termination date (in den Weg gelegt werden wird).” Later documents suggest that Otto left in early October.

Problems about promotion

Max Schultze had moved from Halle to the chair of Anatomy (Ordinarius) in Bonn in 1859, and when Otto gave up his clinical position in order to concentrate on research, Schultze, recognizing Otto’s abilities and his serious commitment, tried to find a position for Otto in Bonn. Early in 1862 Baron de la Valette was suggested as a candidate for a prosector position in Anatomy, and Schultze proposed that such a position should also be offered to Otto. The discussions were protracted (langwierig), as the divided faculty discussed the merits of this suggestion.

Eduard F.W. Pflüger, a student of Johannes Müller, who had been appointed to the Bonn chair in Physiology in 1859, summarized the position as follows: “The proposal that the faculty make the following nomination as Professor Extraordinarius is an honorary signal (Bezeugung) that can have no significant meaning for the teaching or scientific purposes of the University. If such a position is offered to Baron la Valette then it is arguable that Dr. Deiters should share this position, particularly since his (Otto’s) misfortune just now urgently presses on us to act in fairness.” He goes on to say that while all are agreed on this point, some faculty members feel that the best outcome for the two candidates would be obtained from the Ministry if the position were offered to the Baron and Otto were nominated for another University. However, there were no positions available in other Prussian universities, and if there had been, then other, older, equally suitable candidates would qualify. Pflüger and Schultze left no doubt about Otto’s higher scholarly qualifications.

Carl Wutzer, former chief of surgery, but still active, spoke positively about Otto’s activities and personality, sharing Schultze’s positive views, but pointed out that if Otto were appointed, there would be no money for him. “We have no funds for scholarship and the arts (Kunst).” The vote went five to three against Otto (see Deiters, 2006 for details) in favor of de la Valette. Still, the issue was not settled. Pflüger presented strong arguments in favor of nominating both candidates, and Naumann added detailed comments about his careful (vorsichtiges) relationship with Otto, indicating that, yes, there had been misunderstandings, and that he had supported and encouraged Otto’s studies and had often had to attend the clinic in place of Otto. At the time of the father’s death he had made efforts to increase Otto’s income from available clinical funds. For three-fourths of 1861 Otto’s income had been increased by 325 thaler.[27] Although he (Naumann) had been ready to be helpful, he was surprised when Otto

[27]The melt value of a silver thaler today is just over 30 US$, and the value of silver per ounce, which was 1 US$ in 1860, is now around 17 US$, seeming to leave the thaler worth a little less than a dollar today. There are more realistic ways of making such comparisons (see (http://authors.library.caltech.edu/13155/1/HOFjeh02.pdf and also http://www.roiw.org/5/4.pdf), but they will not be explored here. It seems clear that at a time of significant family hardship Otto was giving up a nontrivial part of his income in order to focus on his research.

suddenly announced that in "consideration of his family and his partiality (Vorliebe) for microscopy," he could not stay with the clinic; Naumann had pointed out to Otto that his continuation in the clinic would bring an annual income of 250 thaler. "I had to let him go. I was sorry because I had got used to his friendly face and modest ways."

After an unusually long debate,[28] it was decided to send both names to the Minister, with strong recommendations written for both by Schultze. The Minister accepted the nomination of Baron de la Valette, so far as we can tell without a salary, and rejected that of Dr. Otto Deiters. Otto himself was and would remain bitter about this decision during the brief and busy last two years of his life. In 1874, Baron de la Valette succeeded Max Schultze as head of the Anatomy Department, retiring in 1906. Today the Anatomy Department has a bust of the Baron in the entrance hall but nothing to memorialize Otto (Fig. 5).[29]

The death of Max Deiters

Max Deiters, three years younger than Otto, had started training as a mining engineer/inspector. In November 1861, he sent a copy of his final written work (thesis?) to his uncle who worked in mining and to a fellow student. The latter replied with a strong negative comment about their current career prospects. Earlier Otto had tried to persuade Max to change fields, writing: "Your subject may be a primarily practical one, but in the two years you have to spend in practical work, it is not useful to waste so much time stone-bashing (Steineklopfen). Since you are interested in natural history you could spend your time more usefully." Max wrote to his uncle about the limited career opportunities: there were serious doubts about a career in mining, he still wanted to complete his exams but was not eligible for another 18 months, a medical training was too long to be affordable, so he was thinking of training as a science teacher. He was a lost young man, dependent on his older brothers for support. He died three days after writing this letter, and a letter from Otto to the local chaplain about the site of Max's grave suggests that it was a suicide.

UNTERSUCHUNGEN ÜBER GEHIRN UND RÜCKENMARK DES MENSCHEN UND DER SÄUGETHIRE

Production of the book, and the preface

Otto spent the next two years feverishly working on material for this book. His death, due to Typhus, just over two years after Max's, left the work incomplete. However, the book now represents Otto's major contribution to neuroanatomy because Max Schultze and Hermann Deiters were able to prepare Otto's notes for the printers.

Schultze's preface (pp. V–XVII) describes the exacting and intense work that Otto had been doing for the two to three years before his death: preparing a textbook of neuroanatomy, starting with an account of the nerve cells, supporting cells, and nerve fibers, then describing sections of the spinal cord and brainstem, and aiming beyond to observations of cerebellum and cerebrum. Otto left behind several unusually fine large figures (Plates ODU I-ODU V) that he had occasionally shown to visitors. Schultze mentions hundreds of microscopic preparations, many preserved in balsam, that Otto used in his lectures.[30] His aims were private, and his methods were difficult, owing much to those of Schultze himself. Schultze describes Otto as reserved and uncommunicative, providing colleagues with only occasional, scattered information. Schultze wrote "...anyone who knew Deiters's earlier publications on microscopic anatomy, who knew the perseverance and tenacity with which he aimed at a once established (gestecktes) goal, had to conclude that the difficulty of the chosen methods raised the expectation of significant results. That Deiters over the several years of this work had won such results was rumoured, here and there, but as private (verschlossen) as he was, he hardly spoke about his discoveries, and gave no lectures about his investigations to academic societies."

Otto's notes were rough. Schultze writes that Otto relied greatly on his memory and describes the notes as a *brouillon* (rough draft) written in a careless hand "with flying quill." Much of the microscopic material was drawn but without explanations. Otto had, during the last few months of his life, taught a private course to two advanced students, and one showed some sketches of the material to Schultze. These and the students' notes gave Schultze some sense of what the material contained. Unfortunately, the notes and the original drawings are lost and we know nothing about the originals, other than Schultze's account and the illustrations in the book itself (Plates ODU I-ODU VI)

Schultze worked for several months with Hermann Deiters, reworking the original difficult and rough notes as a printable manuscript. Hermann, who over several years of correspondence must have learnt to decipher Otto's writing, was a teacher of classical languages, with a strong interest in music, who would later make significant contributions to the history of music.[31] For

[28]More of the debate is recorded in Deiters (2006).

[29]There are current plans to dedicate a lecture theatre to Otto.

[30]They could not be traced when we enquired.

[31]His portrait can be seen in the Beethoven Haus in Bonn.

Figure 5. Otto Deiters toward the end of his life, painted by A. Bausch. (We thank Dr. Wolfgang G. Deiters for supplying the photograph.)

Hermann the technical neuroterminology must have been foreign, but one has the impression that, although evidence of the *brouillon* remains, the man of letters and the teacher may have introduced a degree of order, less obvious in Otto's earlier work.

Without this significant effort of Max Schultze and Hermann Deiters, the book would not exist. We would then still hold Deiters in high regard for his earlier publications, but the view provided by the book of a deeply thoughtful and skilful young scientist arguing (with himself) about conclusions to draw from his carefully prepared and studied material would be lost to us, as would the details of his new observations.

For us the book provides a vivid view of the uncertainties that prevailed 150 years ago, upon which many of our current "certainties" have been built in innumerable, mostly small, steps. We lack the space and the historical sense to present the material in relation to what was known at the time. Otto was remarkably bad at citing others; when he did, it was usually cursory, mention of a name, or occasionally a journal title.[32]

A sense of the then contemporary relevant knowledge is best obtained from the 3rd, 4th, and 5th editions of Kölliker's Handbuch (Kölliker, 1859, 1863, 1867). Van Der Loos (1967) and Shepherd (1971) provide many relevant details concerning the nerve cells and Meyer (1971), Clarke and O'Malley (1996), and Finger (1994) about the brain more generally.

Purkinje (1838; cited by Finger, 1994) had described the cerebellar cells that bear his name and illustrated the basal parts of their dendrites; Wagner (1845, 1847) had illustrated the dendrites extending some greater distance from the cell body of sympathetic cells and cells in the electric organ of fish (*Torpedo*); Remak (1855) had described the several processes (dendrites) that leave the large neuronal cell body of the ventral horn cells, and had traced one single, distinctive process (the axon) into the ventral root. Although Brown Séquard (see Finger, 1994) had demonstrated the crossing of the pyramidal tract and of some of the sensory spinal pathways, it had not yet been possible to trace the sensory pathways through their relay stations in the brainstem. Tracing nerve fibers from their cells of origin into their peripheral cranial nerves was still extremely difficult, and the results were often conflicting. Although the demonstration by Bell and Magendie (Finger, 1994) that the spinal dorsal roots are sensory and the ventral roots motor was widely accepted, the connections that might provide a pathway for the spinal reflex remained undefined. The cell theory was still the subject of significant debate and misunderstanding (Baker, 1949; Harris, 1999).

We present Otto's book under several different headings, not in order of the chapters, but summarizing what appear to us as the most interesting points for readers of *The Journal of Comparative Neurology*.

On page XI of the preface, Schultze lists novel observations included in the book: conspicuously the identification of the superior olive in the human brain, previously only reported in animals since it is visible in many mammals, but is hidden in the human brain by the large pons; also the identification of a large-celled gray nucleus between the origin of the inferior cerebellar peduncles that Schultze suggested be called Deiters nucleus (Plate ODU V, Fig. 14). Schultze draws attention to Otto's account of a lateral (intermediate) motor component of the cranial nerves, lying between those corresponding to the spinal dorsal and ventral roots, specifically including the accessory, seventh, and fifth cranial nerves. Schultze describes as a major contribution Deiters's account of nerve cells having a single axon[33] and multiple "protoplasmic processes" (dendrites), with an additional second system of fibers attaching to the dendrites. However, Schultze then

[32]This was typical of his published work as well.

[33]Both Schultze and Otto called the axon an Axencylinderfortsatz, perhaps best translated as axial cylindrical process. The German word Axencylinder- or Achsencylinderfortsatz has a long history, going back to Fontana (1730–1805; see Spillane, 1981) and probably relates to the current term "axon," which has the same Greek root. Otto was clear that each nerve cell had only one such Achsencylinderfortsatz. His occasional use of Hauptaxencylinderfortsatz (principal axon) was meant to distinguish it from the second system of fine Axencylinderfortsätze. Kölliker in 1896 was still using the same term for axons but spelling it Achsencylinder instead of Axencylinder.

argues at length that Otto misnamed the protoplasmic processes because he (Schultze) considered that they are not an extension of the nerve cell's protoplasmic contents. Finally, Schultze draws attention to the fact that Otto reports never having been able to trace a nerve process from one nerve cell into continuity with another nerve cell. This is relevant to the view held by several commentators that Otto was a reticularist, or a precursor of this theory (Shepherd, 1971; Swanson and Swanson, 1995; Albright et al., 2000) and is of interest since Schultze himself had described several olfactory fibers fusing to form a single axon and another member of his department (G. Walter[34]) had published an account of rich fusions of neural processes in the leech, fusions today readily recognized as artefacts (Walter, 1863).[35] Otto mentions this study in the text and reports that he succeeded in persuading Walter to take another look. Unfortunately, Otto died soon after the Walter paper was published and we don't know whether Walter ever did look again.

The methods used (mostly from Chapter I)

We know very little about the microscope Otto used except that it had achromatic lenses (see section on Otto's life in Berlin, above). He worked with tissues from humans, calves, dogs, cats, rabbits, and goats, comparing one species with another, and recognizing that human tissue is never well preserved. He cut his sections in conventional cross sections (see Plates ODU III to ODU VI) but also in planes suitable for following particular pathways. He depended heavily on teasing and manipulating fresh pieces of tissue under the microscope, using different chemicals at different concentrations and different temperatures. He watched the extent to which he could preserve the tissues with some solutions but not others, the rates at which different tissue elements disintegrated (depending on species or solutions), and the extent to which different parts were firm and resistant to manipulation or could be moved, distorted, or separated from each other. He (rightly) distrusted the use of sections for judging the continuity of two processes; he preferred to tease out the finer processes. The figures (especially the first two plates), drawn by Otto himself, illustrate how closely related were his skills at manipulating the tissues under the microscope and his considerable ability as an illustrator. The figures in Plates ODU I and II show nerve cells as a three-dimensional tactile experience with potentially mobile parts, a vision that even the Golgi method does not provide.

[34]Many years later, after Hermann Deiters's daughter Maria Deiters had married Hippolyte Guillery, their children could claim two grand-uncles who had worked in the Bonn Anatomy Department in the early 1860s. Otto Deiters was Maria's uncle, and Georg Walter was Hippolyte's uncle.

[35]It is puzzling that Ramón y Cajal (1954) describes Schultze as a father of the neuron doctrine and treats Deiters as a reticularist (see also Guillery, 2005).

Figures 1–15 from the book appear here on six plates numbered ODU I to ODU VI. We refer to them here by the plate and original figure numbers, e.g., Plate ODU I, Figure 2. Plates ODU I and ODU II show dissections of nerve cells and two glial cells. These two plates represent the most original and striking part of the book. Plates ODU III–VI show sections through different levels of the brainstem: In caudorostral order, they are III, IV, VI, and V. Whereas III is identified as being from a human brain, IV and V are not identified; from the appearance of the pyramids, they may well be from a sheep or a calf. VI, judging from the appearance of the pyramids, is human. The legends are translations of the original legends.

Otto tells how to prepare the carmine stain and the importance of freshness, filtering, and other factors. He notes that the intensity of the reaction varies from one tissue element to another and from one region to another. He argues that different chemical compositions of the parts imbibe the dye differentially, but concludes that strict chemical interpretations are not yet possible. He was impressed by the beauty of the carmine preparations, but warns that carmine can give false views of fibers fusing with each other and states that "The aesthetic gratification (Befriedigung) that some find in such preparations has led, I believe, to the overestimation of their scientific significance" (p. 5). He tried double staining with carmine and indigo blue, hoping that the nerve cells might be red and the connective tissues blue, but found that one dye drove out the other (p. 26).

Otto considers the "elementary parts" of the nervous system (p. 5). In view of his earlier publication on the cell theory, this can be seen as an unsuccessful search for the units that were later to be defined by Waldeyer and fought for by Ramón y Cajal. He cites the relevance of Kölliker's and Kühne's observations of nerve endings on muscle fibers but notes that their methods did not serve to separate/distinguish the neural elements (p. 6).

The nerve cell (mostly from Chapter III)

The "typical" nerve cell

Otto stresses how little we know about even the large, well-recognized ventral horn cells: "If one thinks of the ganglion cell of the ventral horn as being the connection/link between the *ventral roots entering* the spinal cord and the ventral columns that are leading to the brain, one has the simplest function that can be assigned to a ganglion cell" (p. 54; italics added[36]).

[36]This description of the ventral roots as "entering the cord" is puzzling. Otto wrote in German: (Man denke sich hier also z.B. zwischen die in das Rückenmark eingetretenen Vorderwurzeln und die Vorderstränge als die leitenden Bahnen zum [sic] Gehirn eine Verbindung durch die Ganglienzellen der Vorderhörner, so hat man doch die simpelste Function, die man einer Ganglionzelle zuschreiben kann.) Here he is thinking of the connections as he traced them, but not of the direction of the signal, which was then known to travel from the brain through the ventral horn cells to the muscle.

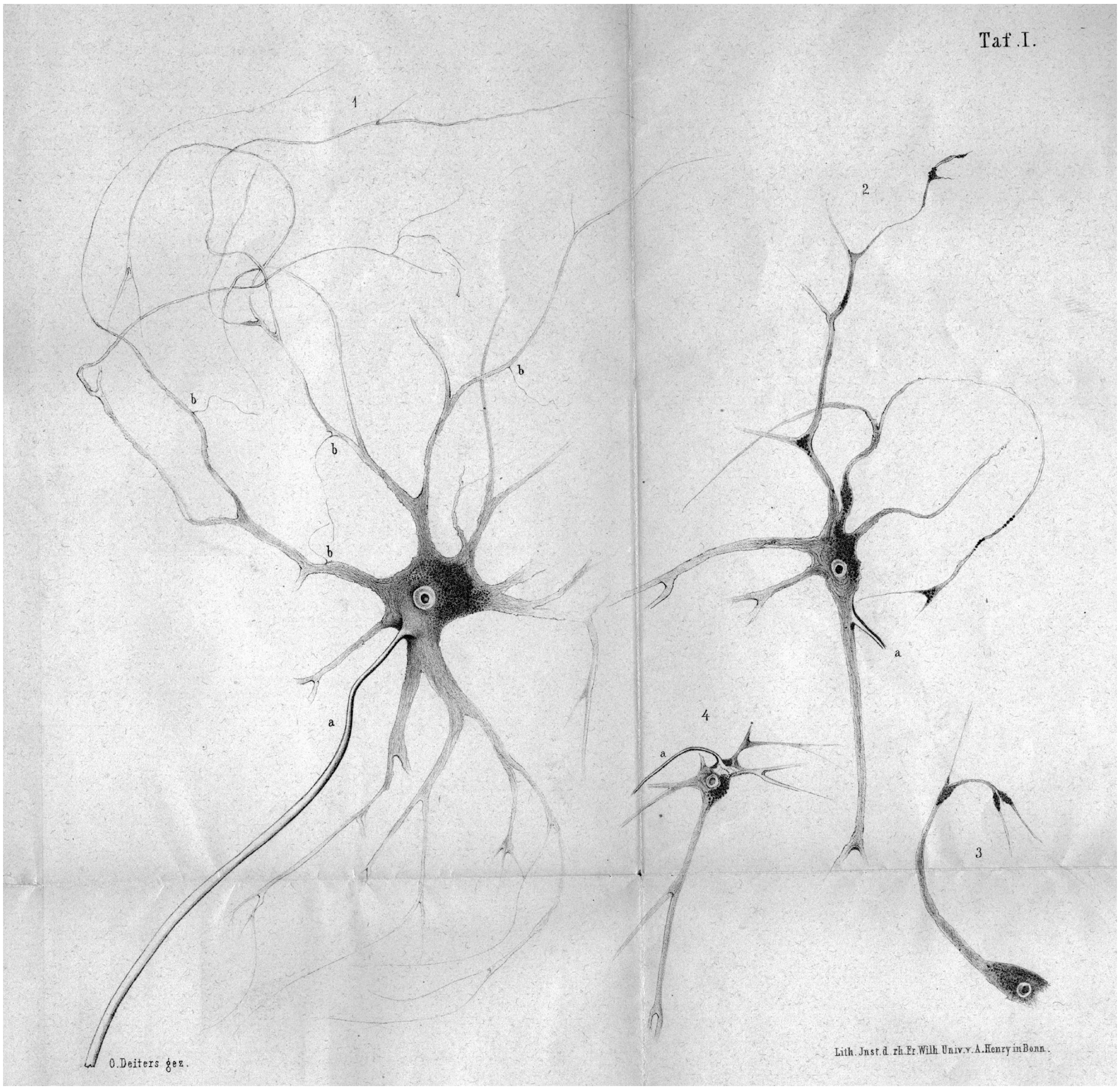

Plate ODU I. The figures in this plate are from the spinal cord gray matter at 300–400 times magnification. (In the book the distance between the nucleoli of cells 1 and 2 is 95 mm.) **Fig. 1:** A large nerve cell from the ventral horn of the spinal cord with the processes possibly completely preserved. In the substance of the cell there are dark yellow pigment deposits. a, the main axon; b, the fine axon processes that proceed from the dendrites (p. 56). **Fig. 2:** A medium-sized nerve cell with much yellow pigment in the cell body and in the dendrites. a, the main axon that arises from the base of a large dendrite, as is characteristic for cells of the dorsal horn. **Fig. 3:** Part of a cell, probably also sensory, with pigment in the processes. **Fig. 4:** A smaller nerve cell with richly branching processes and yellow pigment in the cell body. a, the main axon.

However, he concludes that there is no answer to the question of how the connections from the brain to the muscles are established through the ventral horn cells: "If cells as conspicuous as the ventral horn cells have frustrated us, one can expect much less from the other, smaller cells." He then concludes that our knowledge of nerve cells lacks a solid basis (is "bodenlos").

He describes the typical nerve cell: ". . .it has a central nucleus and enclosed nucleolus, but lacks an identifiable (isolierbare) outer covering or so-called cell membrane separating it from neighboring tissues" (p. 55). "The cell body continues without interruption into a more or less large number of processes that run in long courses, often branching repeatedly, containing granular, often

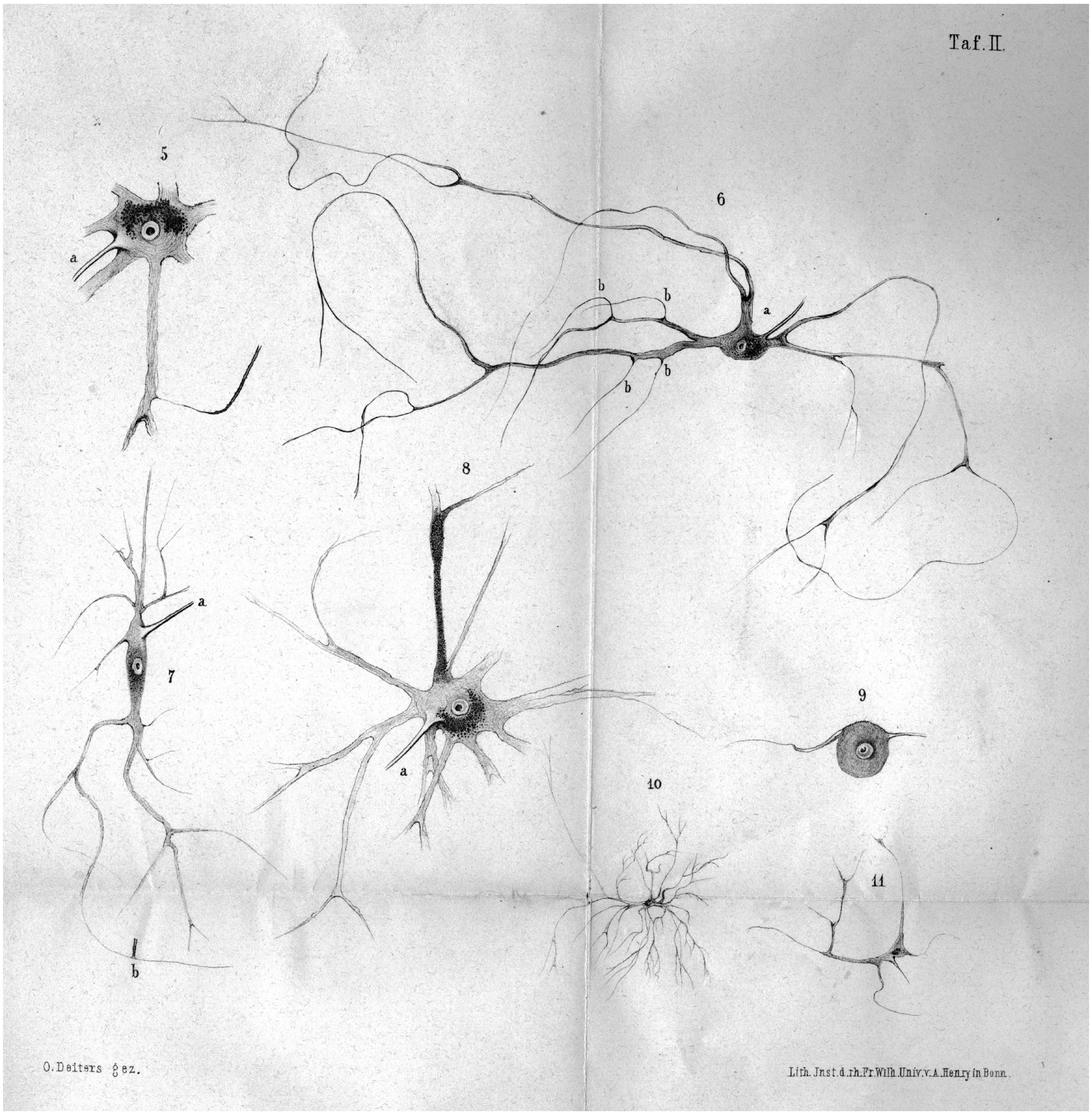

Plate ODU II. **Fig. 5:** A pigmented nerve cell from the gray of the spinal ventral horn. Only one of the dendrites is drawn over some length in order to show the origin of the fine axon b that becomes myelinated. a, main axon. **Fig. 6:** A nerve cell from the dorsal horn isolated with possibly all of its dendrites intact. a, main axon. b, fine axons arising from dendrites (p. 87). **Fig. 7:** A cell of the same sort from the posterior horn. a, main axon, b, a finer axon that is immediately enclosed in myelin. **Fig. 8:** A large cell from the posterior horn that resembles a motor neuron and has a strongly pigmented dendrite. a, main axon (p. 89). **Fig. 9:** An unusual spherical nerve cell such as can be seen near the origin of the trochlear nerve, usually with with two processes, as here (p. 91). **Figs. 10 and 11:** Connective tissue cells from the white and gray substance of the central nervous system. Figure 10 is from the gray of the hypoglossal nucleus.

pigmented protoplasm continuous [with that of the cell body] and extending finally into immeasurably fine processes. . ..For convenience I will call them protoplasmic processes" (the dendrites; p. 56). These are immediately distinguishable from ". . .an outstanding single process that arises from the cell body or, as can occur, from the root of one of the larger protoplasmic processes (Figs. 1, 2, 4A). This single process, 'Nervenfaser-oder Axencylinderfortsatz' (see footnote 33) at its origin can be seen to contain the granular protoplasm. . .but as soon as it

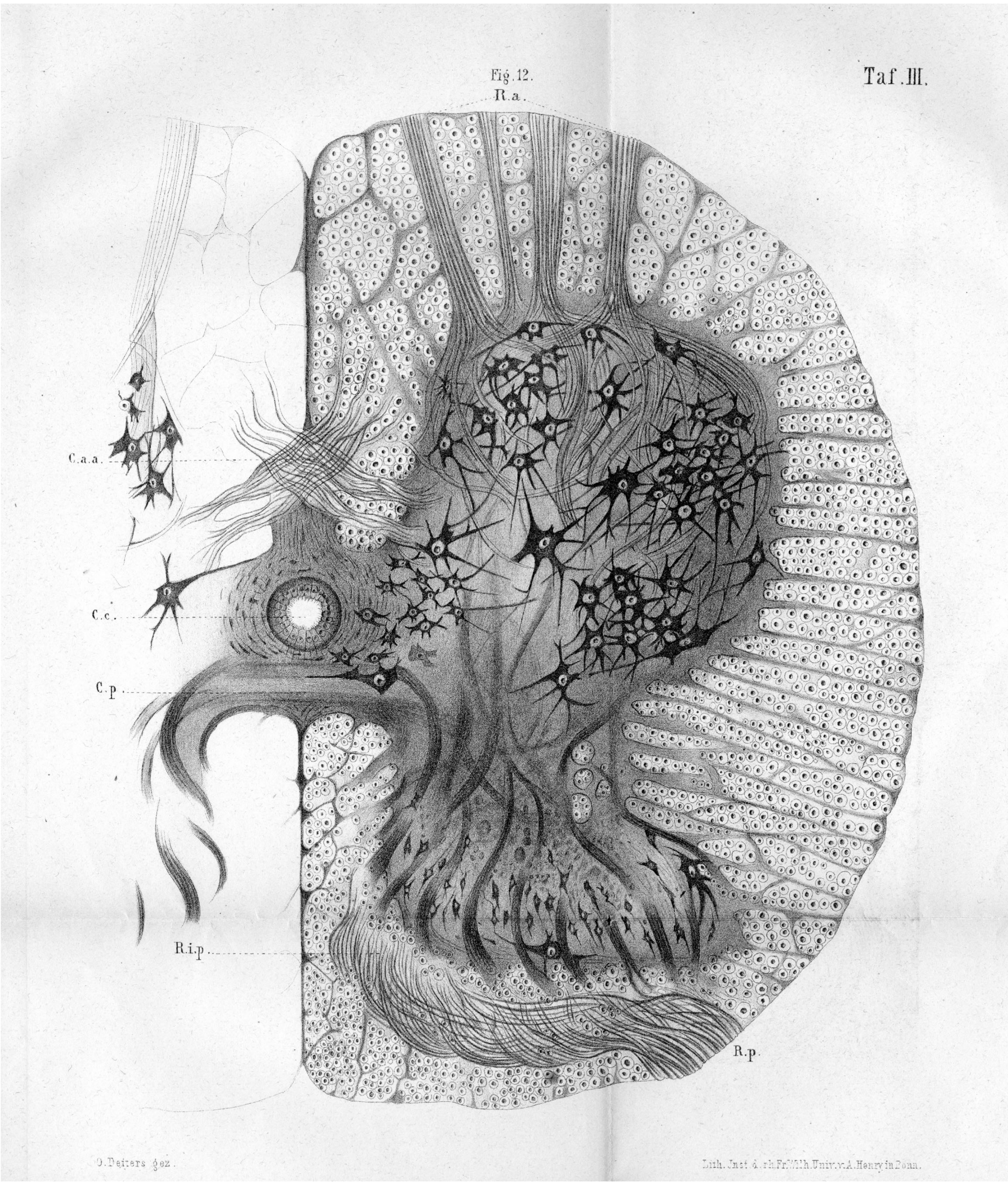

Plate ODU III. **Fig. 12:** Transverse section through half of the lower part of a human spinal cord. Probably near the beginning of the conus medullaris. R.a., bundle of the ventral root arising from the ventral horn within which one can see nerve fibers running among the large cells; R.p., dorsal root leaving the dorsal horn; here the cells are paler and with very few exceptions smaller than those in the ventral horn; R.i.p., inner part of the dorsal root; C.c., central canal with its lining of ciliated epithelium surrounded by connective tissue; C.p., dorsal gray commissure; C.a.a., ventral white commissure. Around the gray horns are myelinated fibers and axons that vary in size in the different regions.

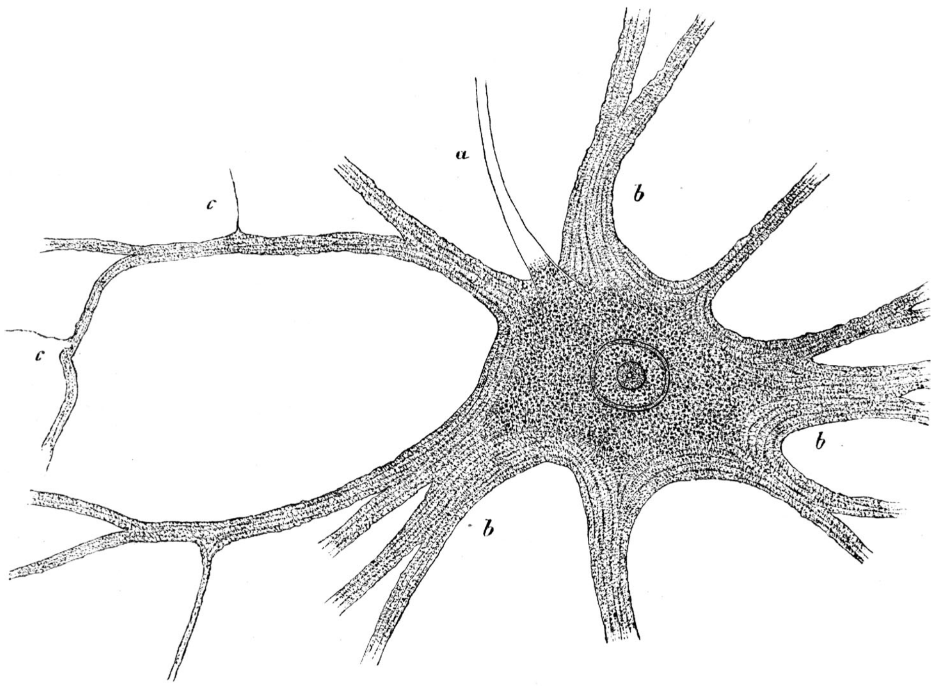

Figure 6. Kölliker's (1867) figure of the second fiber system contacting the dendrites (from p. 276, Fig. 193).

leaves the cell body, a rigid hyaline mass appears that is more resistant to reagents, reacting to them in a quite distinct way, and from its beginning it is unbranched. Shortly after its origin from the cell it becomes thinner (ODU I) (Fig. 1) and usually breaks at this point because of the bend that occurs here." This is the axon, and, here, crucially, he identifies the initial segment for the first time. He describes such nerve cells, with a single axon and several dendrites that branch, in the olive, the pons, and, indeed, in all parts of the brain he has examined including the cerebrum "if I am not mistaken." Wagner (1847) had earlier illustrated cells from the electric lobe of *Torpedo* and distinguished these two types of processes (see Wagner's Figs. 42–44, particularly Fig. 44 in the 1846 publication), but the distinction had not previously been so clearly defined nor had it been broadly generalized for many different types of nerve cells. Remak (1855), as mentioned earlier, had distinguished the single axon from the dendrites for ventral horn cells, but without an illustration. Even after Otto's account had been published, Kölliker (1867), in his Figure 184, showed a ventral horn cell from a human spinal cord that included two short processes "one or the other of which may have been an axon." In contrast to this, Kölliker's Figure 193, here reproduced as Figure 6, shows a single axon and is discussed further in the next section.

The second system of nerve fibers

Otto describes this second system: "On many (protoplasmic) processes of the larger as well as the smaller cells, one sees a number of very fine, easily damaged fibers leaving/coming off (abgehen),[37] which appear not to be simply branches, in so as I far as they sit on a triangular base [see Plate ODU I, Fig. 1]. These processes are very difficult to preserve with their connections, are preserved in only a few solutions, and do not differ from the axons of the finest nerve fibers. . ..They are branched at times, and occasionally I have seen a dark border (myelin) on one of these processes and I don't hesitate to see in these a second system of outgoing nerve fibers, which seem to differ from the above large throughway" (p. 57). In the next paragraph he adds, "I will try in what follows to show that the two

[37]This "abgehen" can be interpreted as implying that the fibers are conducting impulses away from the cell body and has been interpreted in this sense by some historians. However, there is nothing in this part of the text that would allow a clear interpretation regarding the direction of messages. "Abgehende Fasern" here might just be a description of what the cell looked like, not necessarily implying the direction of the message. The later passage makes this clear, as does a comparison with the meanings in footnote 36.

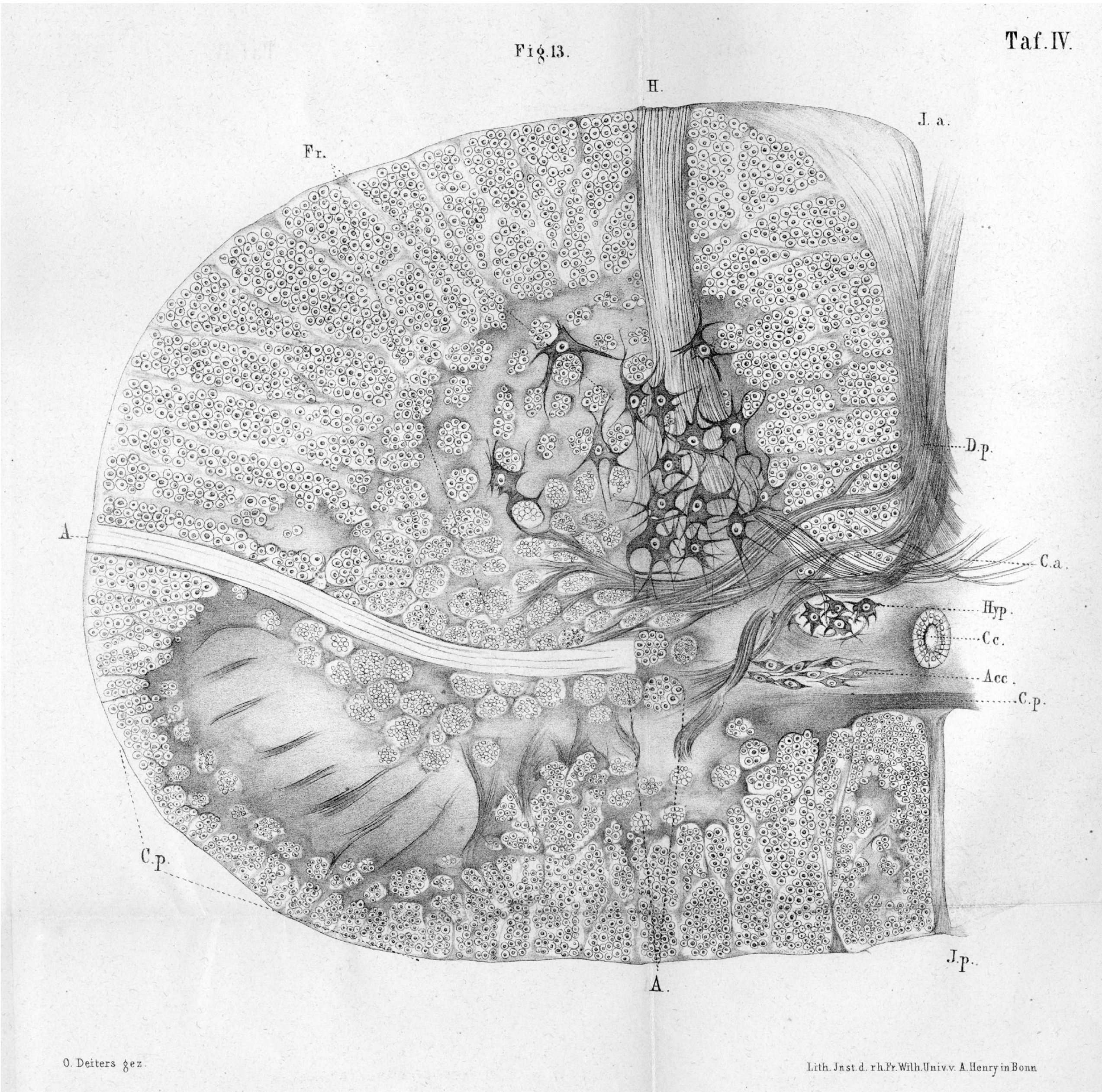

Plate ODU IV. **Fig. 13:** Transverse section through half of the beginning of the medulla, with nerve roots of the accessory and hypoglossal nerves. J.a., ventral fissure, partially filled by the beginning of the pyramidal decussation; C.p., posterior gray commissure; C.c., central canal; F.r., reticular formation, the reticular connective tissue that arises from (is continuous with) the ventral horns and increases to occupy the greater part of the medulla; C.p., posterior horn, at its base also continuous with the framework of the reticular formation; A., accessory nerve; H., hypoglossal nerve; A′., transverse section of the accessory nerve; Hyp., cells of the hypoglossal nucleus.

systems of axons serve two different directions" (das diese beiden Systeme verschiedenen Richtungen angehören).

He returns to the second axonal system, and discusses the possibility that they might contact the cell body as well as the dendrites, stresses how easily they are destroyed, and gives details of how they can be preserved. He says that they are not artefacts; occasionally they can be identified as the unmyelinated end of a myelinated fiber (pp. 64–65; Plate ODU I, Fig.7b). "I am convinced that with careful treatment, as described, the appearances in the figure and my description can be confirmed" (p. 65). Kölliker (1867), who clearly recognized the necessity for some communication involving the dendrites, subsequently illustrated something similar to the fine fibers of the second

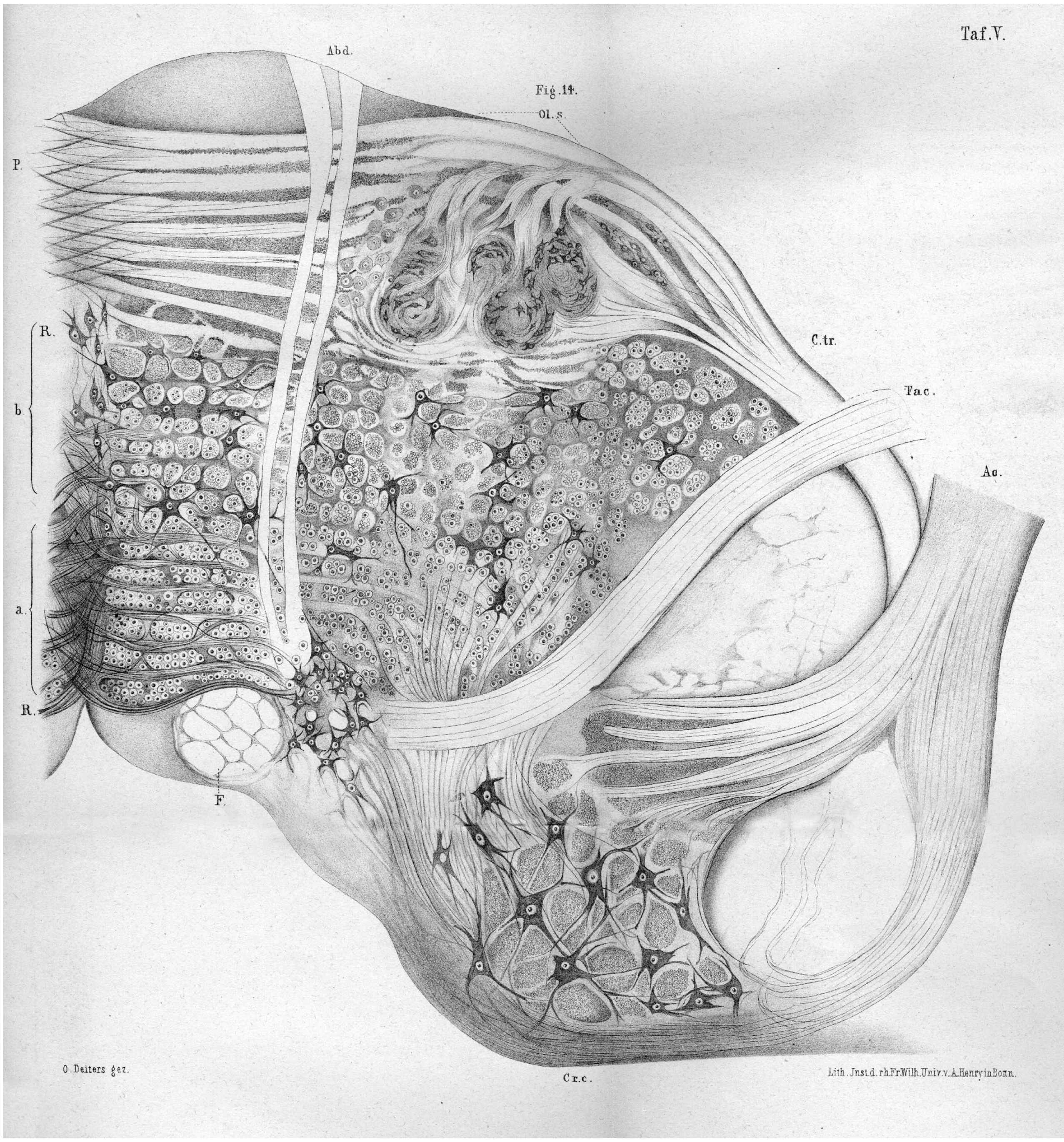

Plate ODU V. Fig. 14: Transverse section through half of the medulla close to its junction with the pons, with nerve roots of abducens, facial, and acoustic nerves. E., fibers of the pyramids[38]; R., raphe—to its right the framework of the reticular formation within whose dorsal portion (part b, smaller) and ventral portion (part a, larger) nerve fibers are found. Ol. (Ol.s.), section through the superior olive; C.tr., fibers of the trapezoid body; Cr.c., inferior cerebellar peduncle with many large ganglion cells that appear to belong to the origin of the acoustic nerve, Ac.; Fac., facial nerve; F., the same cut in transverse section at the facial genu; Abd., abducens nerve. The drawing is incomplete; the transverse sections of the many thick fibers (at J [sic]) should be shown.

system (Fig. 6). He pointed out that he had described them earlier and that he could not distinguish them from the other processes given off by the dendrites. He could not trace any of these into a myelinated stretch, as Otto had shown in Plate ODU I, Figures 5 and 7. Kölliker concluded that the existence of the second system of fibers was "not a decided matter" (Eine nicht abgeschlossene Sache).

[38]This is an error. There is no E in the figure and probably the P was intended.

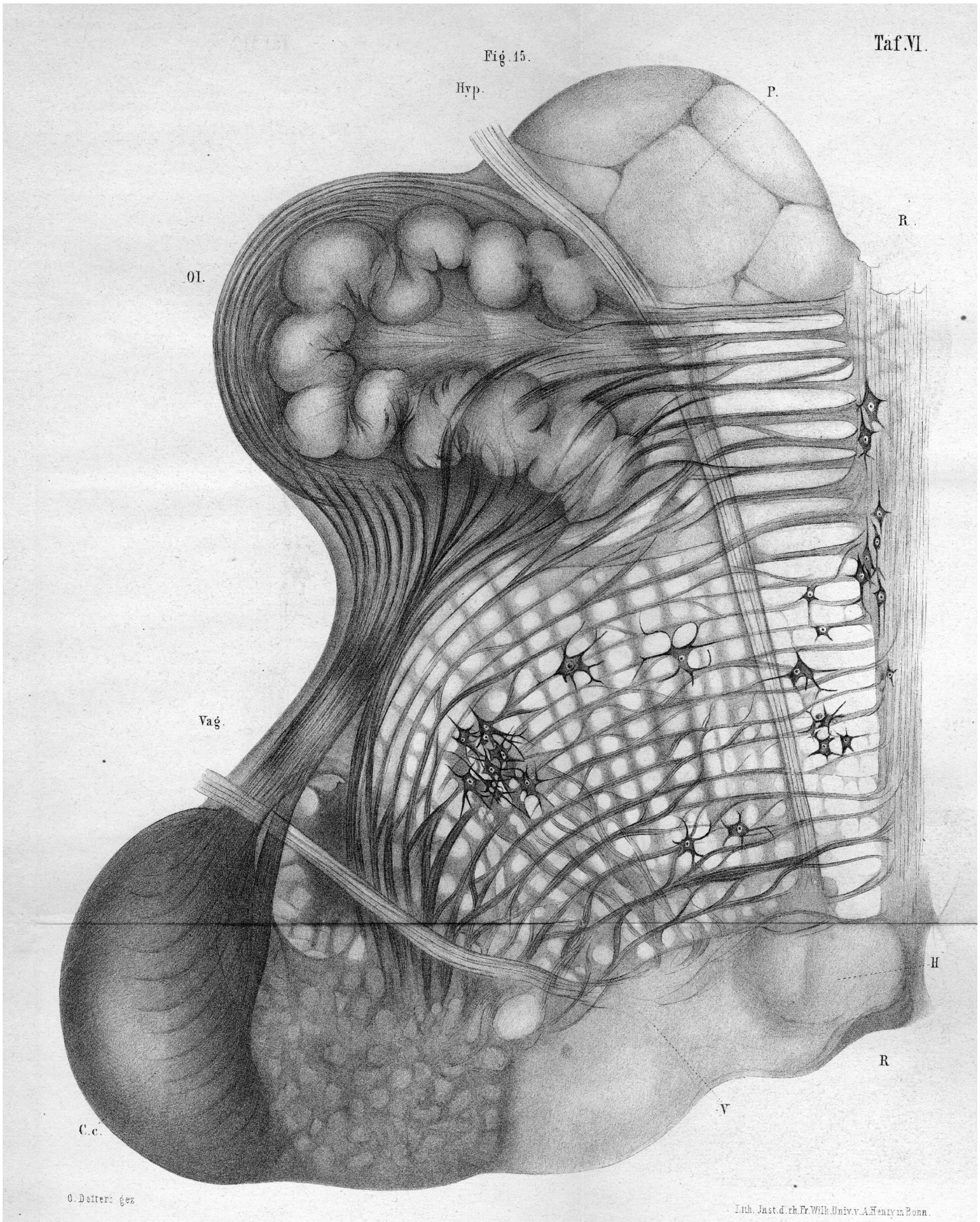

Plate ODU VI. **Fig. 15:** Section of the human medulla at the level of the (inferior) olive (Ol.). R.R., raphe; Hyp., hypoglossal nerve, Vag., vagus nerve, whose nuclei V and H are not drawn in finer detail. The main part of the figure includes the reticular formation with its scattered nerve cells and the olive with its approaching fibers of the stratum zonale; C.c., inferior cerebellar peduncle; P., pyramidal tract.

The fact that Otto had described incoming axons making what we can now recognize as synaptic contacts with the dendrites was not appreciated by later workers and was altogether lost sight of by many. In part this was because the adhesive properties of synapses were not recognized, and in part because when finally, some decades later, synaptic contacts were described light microscopically, they appeared to show a light microscopically visible synaptic gap, which Otto's figures did not show. The fact that the actual synaptic gap was too narrow to be visible with the light microscope was not revealed until it could be defined by electron micrographs as only about 20 nm in width.[39] This now makes Otto's drawing entirely believable, and allows us to see these fine fibers of the second system as ending on the dendrites in synaptic contacts (see also Van Der Loos, 1967). Much later (on p. 145), Otto returns to this second system. He points out that the second system of fibers characterizes sensory as well as motor neurons, and raises the possibility that sensory fibers may open into (eimünden) a motor cell. He recognizes that such a connection has not been demonstrated and that there is (thus) no evidence for an anatomical basis of reflex connections. However, he then suggests: "If there should be specific differences between sensory and motor nerve cells, then they must have a physiological and an anatomical significance from which an effect on the spread and the direction of the current would result, so that, for example, the motor roots [would] connect directly with the axon and the sensory, in contrast, [would] connect to the second fiber system." That is, the dendrites on which the second system forms its triangular contacts would be receiving inputs from the second system.

Here he was postulating a functionally polarized nerve cell, with the second fiber system bringing the afferents to the dendrites, and the axon providing the output. This is a stunning, but fleeting anticipation of the dynamically polarized neuron identified later by Ramón y Cajal and Van Gehuchten. Unfortunately, Otto does not have the actual evidence for such connections and does not return to it. We are left with this tantalizing thought: that he recognized the importance of functionally polarized neuron and saw the second system of fibers as a likely input to the dendrites, with the axon as the output. He would surely have followed this up had he lived.

Classifying nerve cells

On page 86, Otto says that the basic structure of cells in the dorsal horn is the same as in the ventral horn. He does not plan to describe differences in form, size, number, and length of processes and their branching... The cells of the dorsal horn are more difficult to dissect and survive less well but they are basically the same. He refers to the dorsal horn cell that can be seen in Plate ODU I, Figure 6: "On the branches one sees a fair number of the little branches (Reiserchen) [Plate ODU I, Fig. 6b,b] leaving from a triangular basis (the second system of fibers)"[40] (p. 87). That is, nerve cells are generally the same everywhere. On page 90, he says that in the medulla the cells of the accessory, hypoglossal, and vagus nuclei show the same characteristics, with some special features (but they are harder to stain than spinal cells). On pages 94–95, the same basic cell structure is seen in the nerve cells of the inferior olive, pons, and dentate nucleus, in the substantia nigra, and for some cells in the granule cell layer of the cerebellum. The large cells of the medulla only differ from the small cells in their size. Earlier, in the chapter on connective tissues, he considers the "so-called granules in the second layer of the cerebellum. I will show that these so-called free nuclei have structures surrounding the nucleus that form a narrow border of protoplasm that continues into enormously long fibers"[41] (p. 37). He concludes that these are nerve cells, although he says nothing about their dendrites, and he does not return to this issue later in the book.

Only for the cells of the superior olive has he failed to arrive at a clear view of their structure. On page 95, he says that "Finally there is a third cell type scattered in the cerebellar cortex that can continue on both sides as an axon[42]....This strange small cell is one of the few examples of a cell that I have not yet been able to fit into a general schema of nerve cells." In addition, on pages 91–92 he describes cells near the origin of the trochlear nucleus as another exception (ODU II, Fig. 9). He likens them to dorsal root or trigeminal ganglion

[38]This is an error. There is no E in the figure and probably the P was intended.

[39]The reasons for this apparent discrepancy between some of the light microscopic images of a large synaptic gap and the electron microscopic images of a much narrower gap are discussed by Gray and Guillery (1961; and see Guillery, 2006). Essentially, the views of the wider gap were based on reduced silver stains of the neurofibrillary skeleton that left significant parts of the nerve cell unstained.

[40]On page 84 he describes dorsal horn cells whose axons enter the dorsal root, but does not mention the species.

[41]Presumably he traced the axon into a parallel fiber. There is a problem about this statement since in other notes (pp. XI–XII of the Preface), he treats the granule cells as connective tissue elements (glia). Although this account of the granule cells as neurons is definitive in denying that they are glial, and the observations must have been much more difficult than those leading him to see them as glia, we have no way of knowing which observations he would have included in his final account. Certainly, Schultze, citing these notes in the Preface, not knowing what granule cells are really like, took the glial categorization seriously and ignored the other possibility.

[42]Cerebellar fusiform cell?

cells, having hardly any protoplasmic processes. He is puzzled by these,[43] is uncertain about having obtained a complete dissection, and recommends further study by others.

The lack of nerve cell fusions

Otto notes how readily the beauty of carmine-stained preparations can mislead one into interpreting every process of a nerve cell as an axon, and interpreting the complex interconnections as supporting the doctrine of anastomoses between ganglion cells (p. 54). He is entirely clear that such anastomoses are not to be found. Some authors see "the presence of such connections as a physiological necessity[44]. . ..Those who hold these views about the easy and frequent opportunities for observing such anastomoses must have been startled that Kölliker, whose experience and observational skills no one would wish to deny, had never asserted that he had seen one. . ..Every reasonable author working without preconceptions must come to the same conclusion" (p. 67). "I have. . .never seen an anastomosis. . .in preparations whose processes could be followed to their finest ramifications, as in (ODU I) Figure 1" (p. 69).

The nerve fibers

Otto quotes Bidder regarding the absence of Schwann cells in the central nervous system (pp. 101–102). "Many authors opposed this on theoretical grounds, others like Kölliker were doubtful, and others like M. Schultze agreed with Bidder. . ..I must admit that from my studies I have learnt nothing that proved to me the existence of such a sheath, and the ways [for finding a sheath] given by the authors led in the opposite direction." Otto describes that where the axon leaves the nerve cell as an uncovered structure, and where the myelin begins there is no evidence for the beginning of a cover. And, similarly at the nerve ending, where a cover should stop as the myelin stops, there is no evidence of a separate cover (p. 103).

Some generalizations

On page 98, Otto says that "The only thing that I can contribute in relation to this question [classification of cells] is something very insignificant [sic], namely, the fact that the size of the cell body is proportional to the thickness of the axon that leaves the cell body." He notes further that "The arrangement and quantity of nerve cells in a part [of the central nervous system] is in a certain (gewissen) proportion to the nerve fibers with which it is connected." He cites the brachial and lumbar enlargements, the size of the pontine nuclei in relation to the middle cerebellar peduncle, and the trapezoid body in relation to the superior olive.

The connective tissues (mainly Chapter II)

Although Virchow had identified glia earlier, Otto writes about connective tissues and argues (on pp. 29–30) that recent accounts have provided no agreement concerning the differences between neural and supporting elements. At the beginning of Chapter II, Otto is critical: "The central organs of the nervous system have a connective tissue framework (Gerüst), which more or less follows the general form of all parts, is nowhere missing and within whose meshwork the neural apparatus is embedded. When this general statement, which in this form in itself can raise no doubts, is first announced, one might well regard it as an ingenious guess (geistreiche Divination) rather than one supported by stringent observations" (p. 27). He then asks: What can we see to support such generalizations? How can we distinguish between neural and non-neural elements? If we follow Reissner, that "only a connection with an indubitable nerve fiber can identify a nerve cell, then this is an aid that must have the first priority" (p. 28). However, Otto notes, this leads to misinterpretations wherever such continuity is lost.

Most usefully, on page 38 he turns to Max Schultze's study of the retina and compares the non-neural elements of the central nervous system with Mueller fibers. On page 33, he then contrasts white matter cells (which are stellate with many branching processes [Plate ODU I, Fig. 10], presumably fibrous astrocytes) with gray matter cells having sponge-like processes, presumably protoplasmic astrocytes. On pages 44–45, it can be seen that wherever he can trace the cytoplasm of a cell into a neural process this must be neural. Other cells in the white matter have delicate processes, with sharp borders, and a bright appearance. They are easily moved, coil around isolated cells, are not brittle, and branch richly at forked branch points (Plate ODU I, Fig. 10).[45]

Otto argues that many small cells seen in the tissues linking the central canal and pia had been incompletely drawn by Kölliker: "I have no doubt that

[43]Cells of the mesencephalic root of the trigeminal nerve look like this and have been interpreted as displaced trigeminal ganglion cells.

[44]Kölliker (1863) considered fusions between dendrites of ventral and dorsal nerve cells as necessary for producing spinal reflexes, but admitted never having seen such fusions. Otto's comment: "As concerns the argument that physiology demands connections of this sort, I hold that such an assumption does not give us the right to assume particular formulations of anatomical facts, particularly in areas where the unknown dominates."

[45]There can be debate about the identification of this cell as an astrocyte, but we are inclined to accept it as such on the basis of the observations that Otto made as he dissected it.

here one is dealing with genuine nerve cells…and would ask Kölliker to look at this point once more" (p. 33). The possibility of confusion between connective tissues and neural elements seems like a "phantom (Gespenst) of which investigators have allowed themselves to be frightened more than is necessary." Later, on page 36, he notes that "If one starts with the pia to win a secure basis for the parts that can indubitably be described as not neural, then there is a straight path open." Next, he stresses the differences between neural processes and the connective tissues (p. 37).

The spinal cord and medulla (mainly Chapter VI)

In terms of understanding the organization of the medulla, Otto wrote: "here one must deal with concepts about cells and pathways that can hardly be conceived as sufficiently complex….He who concludes that here one is dealing with a thankless task is certainly not wrong" (p. 149). Then he asks: "what is the point of a whole lot of pictures of cross sections if they leave the inner architectonics unexplained?" (p. 150). This is a valid summary of contemporary accounts, which were largely descriptive and offered few organizational principles. He continues that the human medulla is far too difficult and that other mammals provide a much readier view; on the basis of the comparative anatomy, he then provides a useful schematic view of the medulla as first of all a continuation of the basic structure of the cord (pp. 152–156), with the central canal opened as the fourth ventricle, the dorsal columns shifted laterally, and the last 10 cranial nerves continuing the pattern of the spinal nerves. He relates this analysis to the segmental origins of the skull up to the end of the notochord. Second, there is the addition of a third, intermediate column that includes the motor trigeminal, facial, and cranial accessory nerves between the continuations of the dorsal and the ventral columns (later categorized by others as "special visceral efferent"), and, third (on pp. 166–167), the important major modifications that are added to accommodate the connections of the cerebellum. This creates a novel interpretative schema. He traces axons from the inferior olives into the inferior cerebellar peduncle (p. 167) and fibers from the pontine nuclei into the middle cerebellar peduncle.

This general scheme has a surprisingly modern ring to it, and readers of early issues of *The Journal of Comparative Neurology* will recognize indications of an organization for the cranial nerves to which the Journal's earlier volumes made significant additions.[46] We have not found a comparable schematic view in other early accounts (Stilling, 1843, 1846; Wagner, 1845, 1847; Clarke, 1858; Schroeder Van der Kolk, 1859; Reichert, 1859; Henle, 1871), and Kölliker's 3rd edition of his Handbuch (Kölliker, 1859) does not provide a significant source for something comparable, other than recognizing the continuation of the dorsal horn into the medulla and seeing the central gray of the cord as continuing into the floor of the fourth ventricle. The early accounts all provide a fascinating and wonderfully illustrated view of how difficult it was to sort out the separate pathways and components of the brainstem before experimental methods for tracing the pathways became available. However, they do not present a proposed schema of the sort that Otto suggests, beyond Wagner's (1845) recognition of the close relation between the motor trigeminal and the facial nerves.

It is important to note that Otto did not separate the several pathways that cross the midline in the medulla. He treated them as a single "framework" (Balkengerüst), within which the cranial nerve nuclei and other gray masses were embedded. This framework includes what we now recognize as the crossings of the medial lemniscus and the pyramidal tract and all of the other fibers crossing the midline in the medulla and pons including those that link to the inferior olives and the reticular zones of the medulla and pons (p. 226).

"It is wrong to separate the medulla from the pons" (p. 168). Otto points out that the pons varies greatly in size between species so that the ponto-medullary border leaves some pontine structures of the human brain (e.g., the superior olive and the facial nerve) in the medulla of other mammals.

On pages 180–181, he discusses the role of cell groups that interrupt fiber pathways of the "Balkengerüst." These are often seen where pathways turn. "It is possible to consider that the cells only represent a junction (Knotenpunkt) that does not modify the transmission in any way." But his own observations contradict this view: the cell groups "appear all to be the central point of a complicated system of different, complicated fibers, so that there is never a simple through passage or turning point of a fiber" (p. 181). He proposes "a change in the total pattern of currents," one that suggests a synthetic function for the Knotenpunkt. He has in mind "mechanisms (Apparate) that serve as voluntary impulses on moving body parts, on the one hand, or work as perceptual mechanisms for sensory appearances, on the other, and these would thus have sensory functions, and others that can convey stimuli and modify them without serving as direct

[46]See, for example, references in Johnston (1907).

sensory centers." Thus he is suggesting a hierarchy of functions, some simple relays and some with more complex functions relating to the motor and sensory pathways. He is not altogether clear, but he is wrestling with the very real and functionally significant problems of pathways linking the brain to the periphery.

He traces each spinal column into the medulla (p. 185 and onward). This is not altogether in accordance with current views. He includes the large-celled component medial to the inferior cerebellar peduncle (Deiters' nucleus; Plate ODU V, Fig. 14) in the lateral columns and on page 206 connects the dorsal columns, not the lateral columns, to the cerebellum in the inferior cerebellar peduncle, recognizing, however, the enormous contribution that the inferior olive makes to the inferior cerebellar peduncle (p. 167).

Overview

We have condensed 300 pages, written hurriedly and often somewhat confusingly, into a much smaller summary that may, nonetheless, provide a view of Otto's methods of working and thinking. Although his name is still widely recognized in terms of the lateral vestibular nucleus and the supporting cells of the outer hair cells in the cochlea, both named after him, our summary should show that his account of nerve cells as characteristically having a single axon and several dendrites was a far more significant contribution. Individual cells having a single unbranched process (axon) near the cell body and multiple (dendrites) that branch close to the cell body had been described earlier by Wagner (1845, 1847) and Remak (1855), and Otto's generalization of this picture for most nerve cells (with only a few exceptions) was a singular step forward, as was his recognition of the axon's initial segment. The importance of Otto's view of the nerve cell comes into better focus when we appreciate the significance of the second system of nerve fibers with their triangular contacts on the dendrites. These must now be seen as strong candidates for being synapses and arguably the earliest description and drawing of a synapse. His brief reference to the second system as the input to a nerve cell and the axon as the output must serve to demonstrate how carefully Otto had thought about the functional issues, how difficult it often is to formulate new concepts, and how elusive they can be even when they have been formulated a first time. This view of the polarized nerve cell was not raised again until Ramón y Cajal formulated a clear view of the polarized neuron many years later after studying the olfactory pathway and the cerebellar Purkinje cells, where the newer Golgi method revealed the inputs and outputs much more clearly than Otto could see them in the spinal cord.

Otto's account of the changes that occur as the spinal cord broadens out into the medulla and pons and of the hints that comparative anatomy and the segmental anatomy of the skull provide for understanding how the anatomy of the brainstem relates to that of the spinal cord, and how the columns of the cranial nerve nuclei relate to the spinal nerves, represents another area in which Otto sounds remarkably modern.

We have attempted to show Otto's unusual scientific achievements in relation to his difficult family and personal life. It is a sad story that will, we hope, speak to the reader without further comment from us.

The illustrations

It is worth adding a brief extra note on the illustrations. This is not to stress how skilled an illustrator Otto was, which should be obvious, but to draw attention to the extent to which the illustrations themselves, with their three-dimensional shading and their curved processes occasionally crossing over each other, reflect Otto's methods. He had moved these processes about, had judged how flexible, how friable, how tough or delicate they were. These were dead cells, but they differed from the cells that many of us have studied over more recent years: cells that were passive, preserved in the sections for us to view. Otto had actively explored these cells, and the drawings give some indication of this. The Deiters cell portrayed in ODU I Figure 2 shows the scale on which he worked, as do his published drawings (Plates ODU I and I, Figs. 1–15), in which the large ventral horn cell (Plate ODU I, Fig. 1) was probably about 50 μm in diameter and the finer dendritic branches 1–2 μm in diameter. These methods were also used by some of his contemporaries, although most relied on sectioned material more than Otto did, and he seems to have taken these methods further than most others.

CONFLICT OF INTEREST STATEMENT

There is no conflict of interest related to this article for either of the authors.

ROLE OF AUTHORS

VSD summarized the family correspondence, the university documents relating to Otto's departmental appointment, and some of the published research (see Deiters, 2006). RWG summarized some of this material in English, added details about the research, and worked with VSD on difficult parts of the original German texts.

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