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COVER EDITORIAL

The seminal contributions of Benedict Stilling (1810–1879) to neuroanatomy

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Abstract
Benedict Stilling (1810–1879), was a prolific, prominent, and ambitious anatomist, who performed works on the organization of the nervous system for many years. He made numerous observations on the anatomy of the nervous system in various animal species. Stilling contributed to the establishment of significant foundations in the anatomy of the spinal cord, brainstem, and cerebellum. Stilling paved the way for future researchers by describing the techniques he used in his diligent studies published in his published books. In his books, which include many drawings and cadaveric images, he revealed the relationships between the structures in the nervous system. He also made significant contributions to neuroanatomy terminology by coining terms in these books. At the same time, some nuclei in the anatomy of the nervous system were later named after him as an eponym by many researchers. Therefore, Stilling's neuroanatomical works, which are still important today, should be appreciated. This article aims to emphasize his pioneering work in neuroanatomy.

Keywords Benedict Stilling · Brainstem · Cerebellum · Neuroanatomy · Spinal cord · Stilling's nucleus

Introduction

German anatomist, surgeon, and researcher Benedict Stilling (1810–1879) (Fig. 1) was born on 22 February 1810 in the town of Kirchhain in Hessen as the son of a wool merchant [1]. He decided on his future profession when he was 6 years old, because he was influenced by the town doctor who treated his brother's injured hand [1]. Stilling started the Gymnasium at the age of fourteen. When he was eighteen, he was admitted to the University of Marburg [2]. He graduated with his dissertation in Latin titled *De pupilla artificiali in sclerotica conformanda* from the University of Marburg in 1832 [3, 4]. A year later, Stilling, whose sole desire was to be a professor of surgery, became Professor Ullmann's assistant at the surgical clinic in Marburg [1]. In the fall of 1833, at the age of 23, he was appointed as a surgeon to the district court (Landgerichts-Wundarzt) in Kassel [1, 3]. In 1837, he performed his first ovariotomy by using an extraperitoneal technique to avoid internal bleeding [3, 5]. Stilling described this technique in detail in his book titled *Die Extra-Peritonäal-Methode der Ovariotomie* [6]. He married Minna Büding in 1838, and the couple had two sons, Jacob and Heinrich [5]. Jacob Stilling was an ophthalmologist and is known for Stilling-Turk-Duane syndrome. Heinrich Stilling became a pathologist [5, 7]. In 1840, Stilling was forced to transfer to Eiterfeld due to the jealousy of his colleagues in Kassel [1]. He was dismissed from the civil service for refusing to accept his transfer to Eiterfeld [1, 3]. Besides, he could not acquire an academic position throughout his life, being a Jewish [3]. Nevertheless, he carried out his scientific studies himself without the support of any academic institution [1].

Stilling traveled to Paris, London, and Italy between 1843 and 1858. Thus, he became friends with many scientists such as Claude Bernard, Brown-Séquard, and Rayer [3, 5]. His attendance in the meetings of *the Society of German Natural Scientists and Physicians* (Gesellschaft Deutscher Naturforscher und Ärzte (GDNÄ)) increased his scientific reputation

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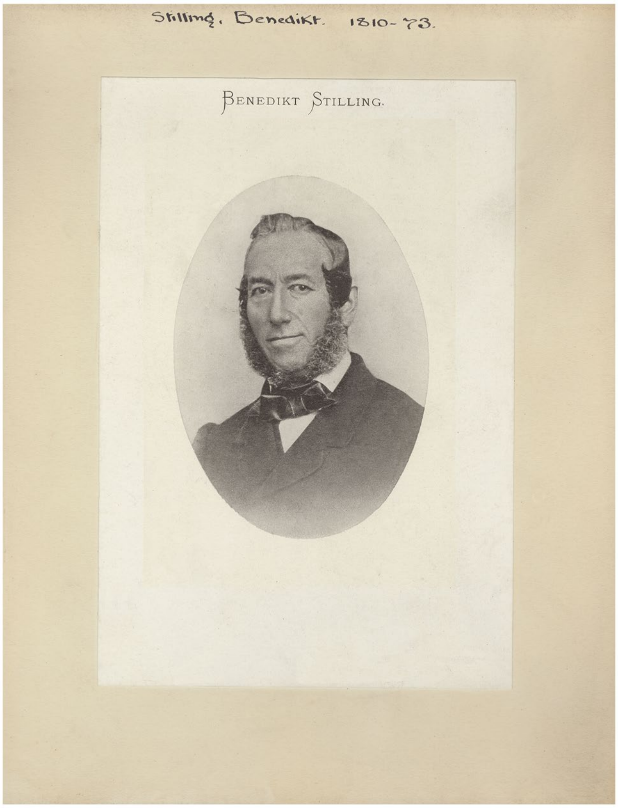


Fig. 1 Benedict Stilling [48]

[8]. In 1865, by reason of his successful publications, he was elected fellow of the German National Academy of Sciences Leopoldina (Nationalen Akademie der Wissenschaften Leopoldina) [9]. GDNÄ elected Stilling as president at its meeting in Kassel in 1878 [5, 10].

He died in Kassel on 28.01.1879 [3], after publishing more than 2500 pages and dozens of figures on the nervous system. Knoblauch [10] stated that Stilling was patient and persevering, and he worked not only for current but also future generations. Benedict Stilling has made notable contributions to several fields, with his research interests and publications covering a wide variety of subjects. However, in this article, we aim to emphasize Stilling's works on neuroanatomy in particular.

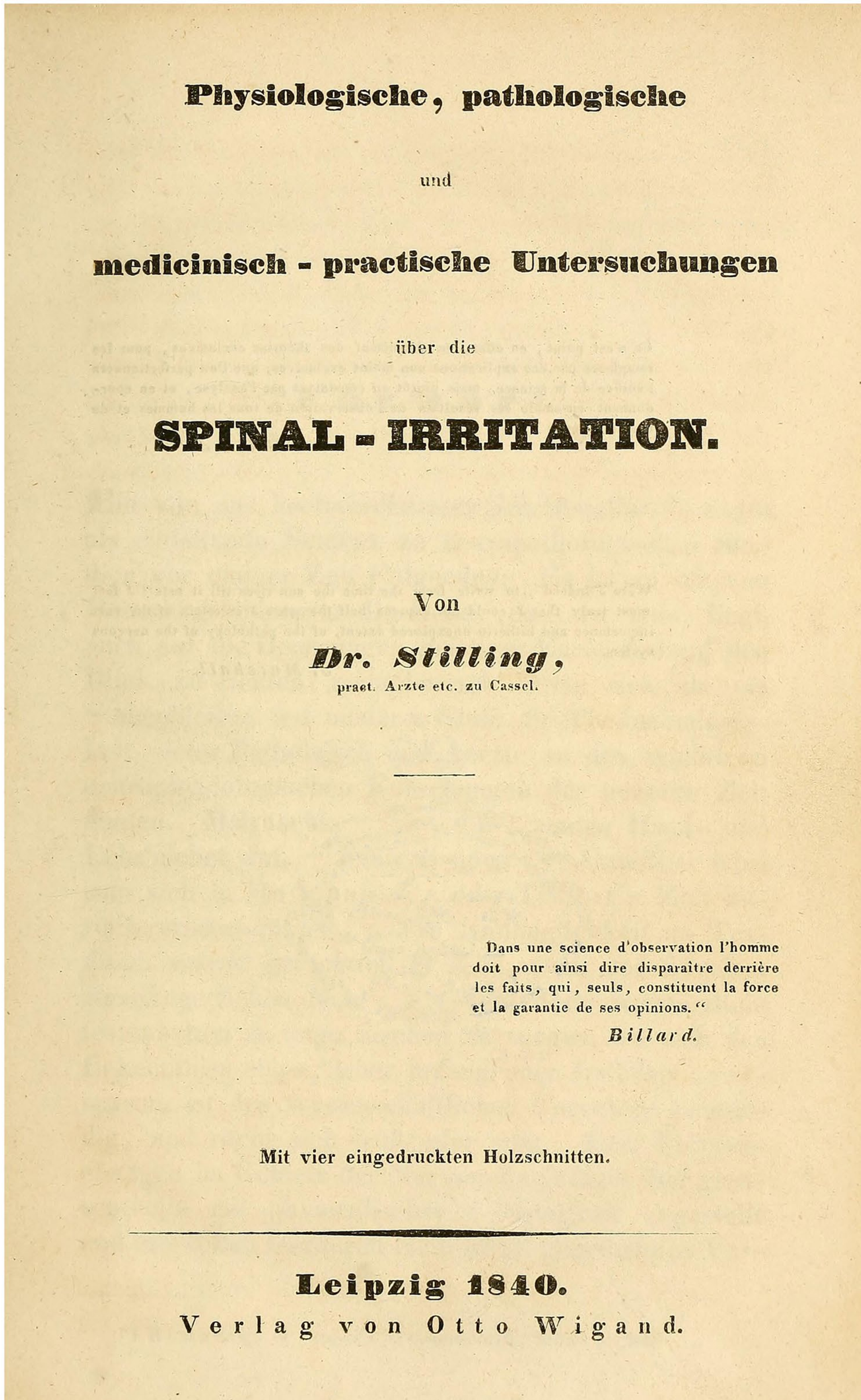
His works on neuroanatomy

Stilling performed significant anatomical, histological, physiological, and surgical research on the organization of the nervous system and published many books on them (Table 1). He especially worked on the anatomy of the brainstem, cerebellum, and spinal cord for many years, and he coined significant terms for neuroanatomy terminology as a result of his observations. His first book on neuroanatomy titled *Physiologische, pathologische und medicinisch-practische Untersuchungen über die Spinal-Irritation* (Fig. 2) was published in 1840 [11]. This book was a prelude to his spinal cord research, and he

Table 1 List of Benedict Stilling's publications on neuroanatomy [1, 5]

Year	Title of publication
1840	*Physiologische, pathologische und medicinisch-practische Untersuchungen über die Spinal-Irritation*
1842	*Untersuchungen über den Bau des Nervensystems. Vol 1 titled Untersuchungen über die Textur des Rückenmarks*[a]
1842	*Untersuchungen über die Functionen des Rückenmarks und der Nerven*
1843	*Untersuchungen über den Bau des Nervensystems. Vol 2 titled Untersuchungen über die Textur und Function der Medulla oblongata*
1846	*Untersuchungen über den Bau und die Verrichtungen des Gehirns. Vol 1 titled Ueber den Bau des Hirnknotes oder der Varoli'schen Brücke*
1856	*Anatomische und mikroskopische Untersuchungen über den feineren Bau der Nerven-Primitivfaser und der Nervenzelle*
1859	*Neue Untersuchungen ueber den Bau des Rückenmarks*
1864	*Untersuchungen über den Bau des kleinen Gehirns des Menschen. Vol 1 titled Über den Bau des Züngelchens und seiner Hemisphären-Theile*
1865	*Atlas photographischer Abbildungen zu den Untersuchungen über den Bau des kleinen Gehirns des Menschen. Vol 1 titled Untersuchungen über den Bau des Züngelchens und seiner Hemisphären-Theile*
1867	*Untersuchungen über den Bau des kleinen Gehirns des Menschen. Vol 2 titled Untersuchungen über den Bau des Centralläppchens und der Flügel*
1867	*Atlas photographischer Abbildungen zu den Untersuchungen über den Bau des kleinen Gehirns des Menschen. Vol 2 titled Untersuchungen über den Bau des Centralläppchens und seiner Hemisphären-Theile*
1878	*Untersuchungen über den Bau des kleinen Gehirns des Menschen. Vol 3 titled Untersuchungen über den Bau des Bergs und der vorderen Oberlappen, sowie über die Organisation der centralen weissen Marksubstanz des Cerebellum und ihrer grauen Kerne und über die centralen Ursprungsstätten und Bahnen der Kleinhirn-Schenkel, nämlich der Binde-Arme, Brücken-Arme und der strickförmigen Körper*

[a]Stilling collaborated with Joseph Wallach in this work


Physiologische, pathologische

und

medicinisch - practische Untersuchungen

über die

SPINAL - IRRITATION.

Von

Dr. Stilling,

pract. Arzte etc. zu Cassel.

Dans une science d'observation l'homme doit pour ainsi dire disparaître derrière les faits, qui, seuls, constituent la force et la garantie de ses opinions. "

Billard.

Mit vier eingedruckten Holzschnitten.

Leipzig 1840.

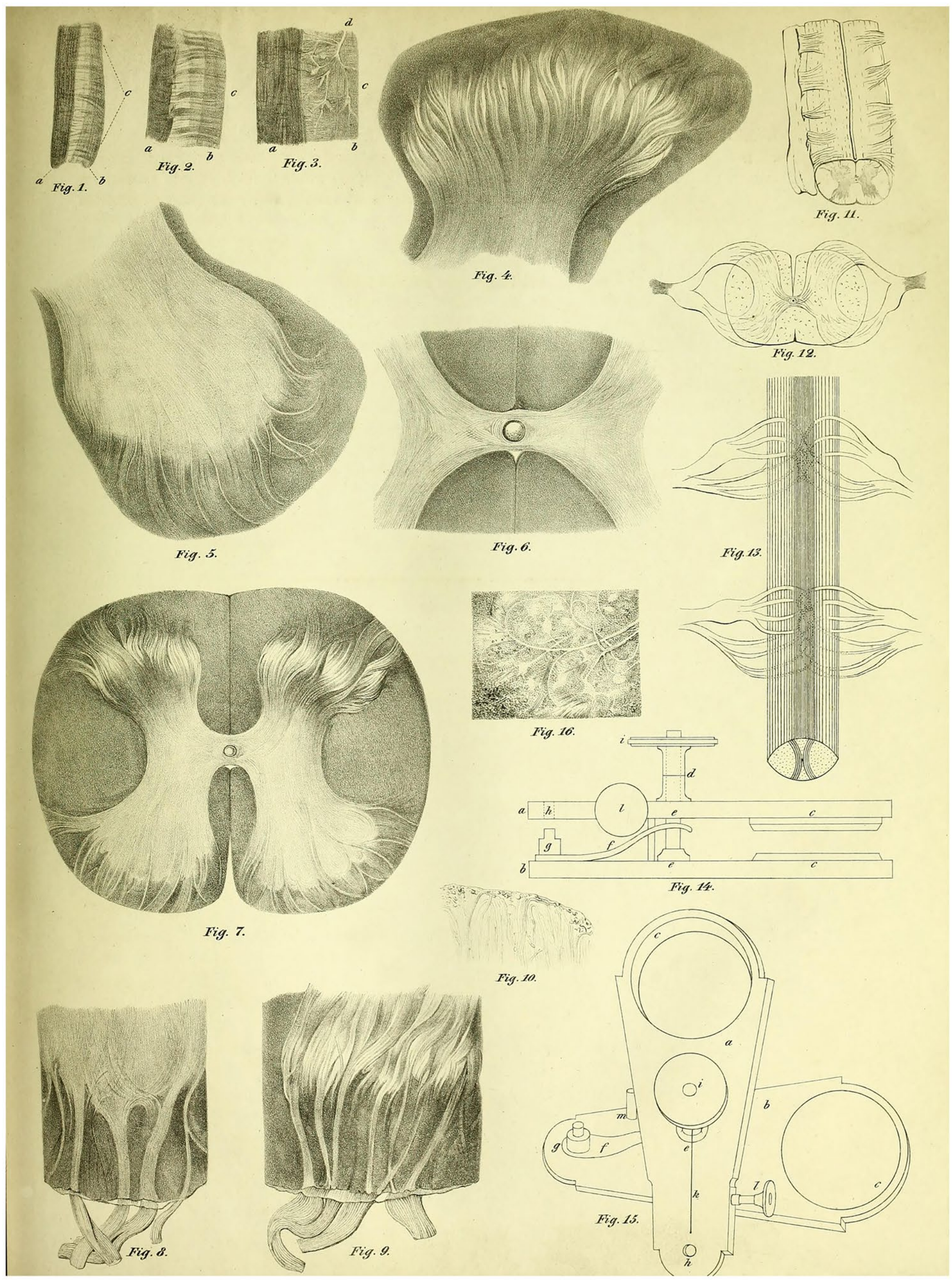
Verlag von Otto Wigand.

Fig. 2 Title page of *Physiologische, pathologische und medicinisch-practische Untersuchungen über die Spinal-Irritation* [11]

postulated that nerves had an influence on arteries, veins, and capillaries in this book [2]. He introduced the term vasomotor nerves (vasomotorischen nerven) which corresponds to the sympathetic trunk [2, 3, 12, 13].

Benedict Stilling is known as one of the first to use serial sections in the nervous system [2, 14]. In 1842, Stilling collaborated with Joseph Wallach to investigate the internal structure of the spinal cord. He was able to cut the spinal cord, which was frozen or alcohol-hardened, using a wide, sharp, and hollow ground razor. He remained visible the reflection of the razor's surface through the section and always wetted it with alcohol. Thus, he obtained serial sections in transverse, longitudinal, and oblique planes of the spinal cord [2, 5, 15, 16]. Besides, he used a compressor invented by Wallach, which he described in detail with his drawings in the book (Fig. 3) [15]. He then examined serial thin sections without histological staining under the microscope (Fig. 4) [17, 18]. Due to this method, Stilling was able to reveal the fine structure of the spinal cord with previously unknown details [5]. Schiller [2] described this new technique as "the peak of microscopic assiduity". Stilling and Wallach subsequently collected their observations in the book titled *Untersuchungen über die Textur des Rückenmarks*. In this book, Stilling [15] stated that he used the fresh spinal cord, preferably from calves, as it is hard allowing to cut thin layers transversely and longitudinally. However, Stilling [15] also investigated the spinal cords of other animals such as pig, frog, and human. Thus, he performed comparative spinal cord research. Later, in 1843, Stilling published his book titled *Untersuchungen über die Textur und Function der Medulla oblongata*. In this book, there are many transverse section figures from the origin of

Fig. 3 Some images, drawings of the calf spinal cord, and Wallach's compressor [15]



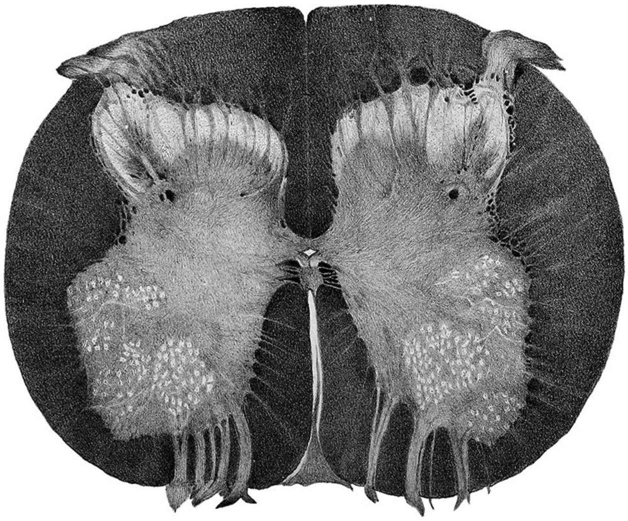


Fig. 4 (Cover figure) A spinal cord section, prepared by Stilling and Wallach [15]. The gray matter, white matter, and fibers from the horns of the gray matter to the anterior white matter can be easily distinguished

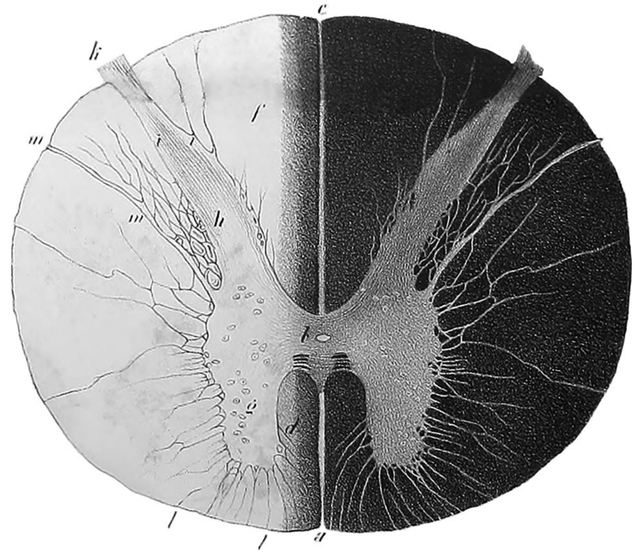


Fig. 5 C3-C4 segment section in the human spinal cord, prepared by Stilling [19]. The terms used by Stilling, and the current usage of the regions corresponding to these terms in the second edition of *Terminologia Anatomica* [47] for this figure are as follows: *Vordere Längsspalte* (anterior median fissure of spinal cord, **a**), *canalis spinalis* (central canal, **b**), *Hintere Längsspalte* (posterior median sulcus of spinal cord, **c**), *weisse Vorderstränge* (anterior funiculus, **d**), *weisse Seitenstränge* (lateral funiculus, **e**), *weisse Hinterstränge* (posterior funiculus, **f**), *graue Vorderstränge* (anterior horn of spinal cord, **g**), *graue Hinterstränge* (posterior horn of spinal cord, **h**), *gelatinöse Substanz* (gelatinous substance of posterior horn, **ii**), *hintere Wurzeln der Spinalnerven* (posterior roots of spinal nerves, **kk**), *vordere Wurzeln der Spinalnerven* (anterior roots of spinal nerves, **ll**), *nervus accessorius* (spinal accessory nerve, **m**)

the 2nd cervical nerve pair up to the pons. Stilling aimed to reveal the difference between the spinal cord and medulla oblongata by presenting in detail the anatomical structures in his figures (Figs. 5 and 6) [19].

Sixteen years later, Stilling published his book titled *Neue Untersuchungen uber den Bau des Rückenmarks* [20]. Stilling, in this book, aimed to overview the structure of the spinal cord and the relationship of its individual parts to one another [16, 20]. The book contains many measurements related to the anatomy of the spinal cord and these were presented in tables. As an example, there are tables where he compared the largest dimensions of the central canal from left to right and front to back in each segment of the ox, calf, and human spinal cord hardened in chromic acid.

In the early nineteenth century, many researchers contributed to anatomical nomenclature. In 1824, Italian anatomist Luigi Rolando published in his book titled *Ricerche anatomiche sulla struttura del midollo spinale* [21]. In this book, he stated that there was a more gelatinous ("più gelatinosa") region in the posterior part of the gray matter compared to the other gray matter regions [21, 22]. He described this region as gelatinous-appearing posterior gray substance ("sostanza cinericcia posteriore d'aspetto gelatinoso") or "posterior gray substance darker and almost gelatinous" ("sostanza cinericcia posteriore quasi gelatinosa e più oscura") [13, 21, 22]. In 1838, Remak used the term substantia gelatinosa as synonym the terms described by Rolando [22, 23]. In 1842, 1843, and 1856, Stilling used the term ''gelatinöse substanz'' (Fig. 5), and he stated that it is situated in all segments of the spinal cord [15, 19, 20, 22].

Fig. 6 An alcohol-hardened medulla oblongata section, prepared by Stilling [19]

Stilling is credited for his research on the brainstem and cerebellum, as well as on the spinal cord. He published the first, second, and third volumes of the book titled *Untersuchungen über den Bau des kleinen Gehirns des Menschen* between 1864 and 1878 [24–26]. Stilling dedicated the book to French physiologist Claude Bernard [25]. This book is about the anatomy of the human cerebellum and brainstem, and its atlases published in 1865 and 1867 contain 126 cadaver images with detailed descriptions (Fig. 7) [27, 28]. As a result of his meticulously carried out dissections, he first distinguished the four cerebellar nuclei of the human cerebellum [29]. He described the fastigial nucleus as ''*dachkern*'' the emboliform nucleus as ''*pfropf,*'' the globose nucleus as ''*kugel-kern*,'' and the dentate nucleus as ''*corpus dentatum*'' [24–26]. He also distinguished ''*vincingulum lingulae*,'' a term in

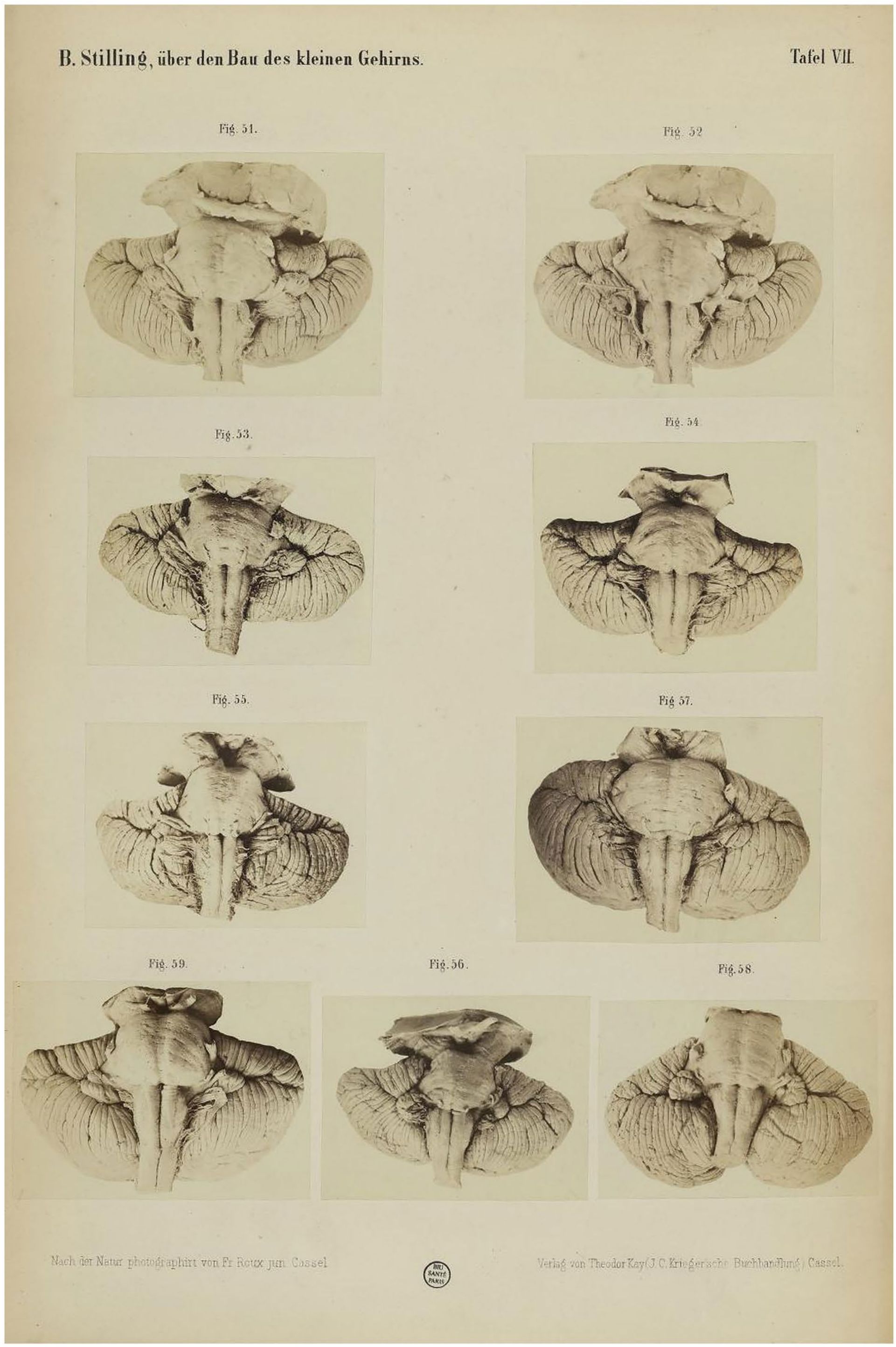


Fig. 7 Cadaveric images of the cerebellum and brainstem, prepared by Stilling [27]

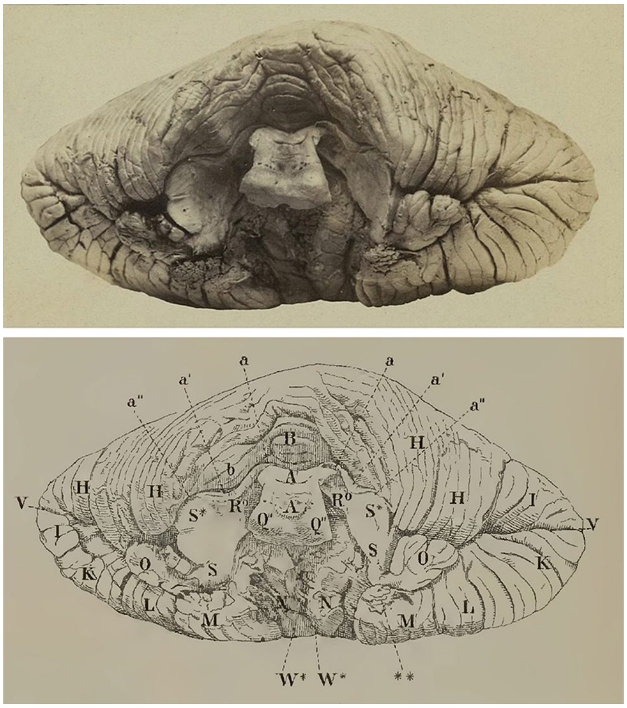


Fig. 8 A cadaveric image of the cerebellum and an illustration of the same image, prepared by Stilling [27], *zungenbänder* (**a**)

terminologia neuroanatomica [30], from other structures in the cerebellum as *zungenbänd*. (Fig. 8) [25, 31].

Stilling's nuclei

The central nervous system has a large number of nuclei identified by many scientists at various times. Schiller [2] stated that German physician Johann Christian Reil used the term ''nucleus'' to the basal ganglia; however, Stilling expanded the term and applied it to cranial nerves. Thus, the term had been acquired a universal meaning by Stilling [13, 32], and the widespread use of the term has significantly influenced neuroanatomy terminology. As early as 1843 and 1846, he described the nucleus of oculomotor nerve, nucleus of trochlear nerve, and motor nucleus of trigeminal nerve [2, 15, 32]. The gray matter of the spinal cord is known to have many nuclei, such as the central cervical nucleus, intermediomedial nucleus, and sacral dorsal commissural nucleus [33].

The dorsal nucleus is one of the nuclei in the gray matter of the spinal cord [34, 35]. In 1851, British physician Jacob Augustus Lockhart Clarke first defined the dorsal nucleus as the posterior vesicular column (Fig. 9) [36]. After that, Stilling introduced the dorsal nucleus (dorsal-kern) term instead of the posterior vesicular column, because it is located dorsal of the spinal cord [20]. Over time, the dorsal nucleus was named with many different names by researchers.

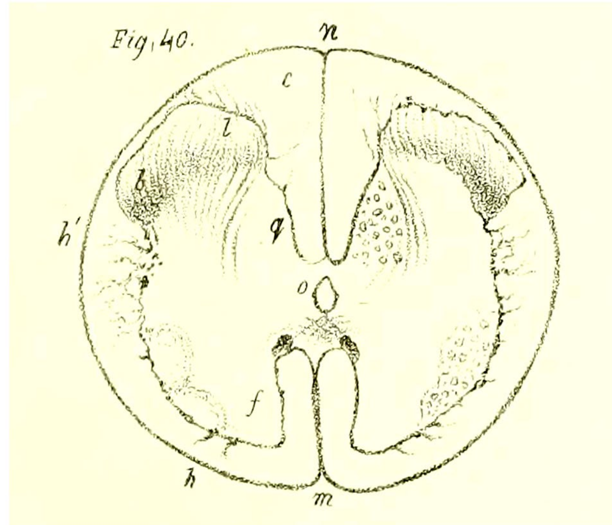


Fig. 9 A transverse section of lumbar region in the spinal cord of a 6-month human fetus [49], posterior vesicular column (**q**)

Waldeyer-Hartz used the term Stilling's cells or cells of Clarke's columns (Stilling'schen Zellen oder Zellen der Clarke'schen Säulen) instead of the dorsal nucleus in 1889 [37]. Koelliker preferred to use the term Clarke's column or Stilling's nucleus (Clarke'sche säulen oder Stilling'scher Kern) in 1896 (Fig. 10) [38]. The most commonly used terms nowadays are the dorsal nucleus, Clarke's nucleus, or Clarke's column.

The dorsal nucleus is found at segmental levels T1-L3 in most animal species [35], and Stilling's sacral nucleus is generally considered to be a caudal extension of the dorsal nucleus [39]. However, it is known that the cells in Stilling's sacral nucleus differ from the cells of the dorsal nucleus in terms of size and cytoarchitecture [39]. In 1951, Chang [39] described a group of cells that appears to be a caudal extension of the dorsal nucleus in spider monkey. In 1977, Petras described it as cells of Stilling (St), the cell population that is a continuation of the dorsal nucleus in the sacral cord of the rhesus monkey, and he noted that his findings corroborate Chang's results [40].

In 1978, Snyder et al. [41] stated that Stilling's sacral nucleus existed in the rat and squirrel monkey, and noted that neurons of Stilling's sacral nucleus projected to the contralateral cerebellum, but neurons of the dorsal nucleus projected to the ipsilateral cerebellum. It is also worth pointing out that, although the term Stilling's nucleus is used for the dorsal nucleus in the spinal cord, over time, some authors also used this term for other cell groups such as the red nucleus, and nucleus of hypoglossal nerve [42, 43]. However, the terms ''*Stilling's nucleus*'' or ''*Stilling's sacral nucleus*'' are commonly used nowadays for the sacral precerebellar nucleus, which is located in the sacral segments [35].

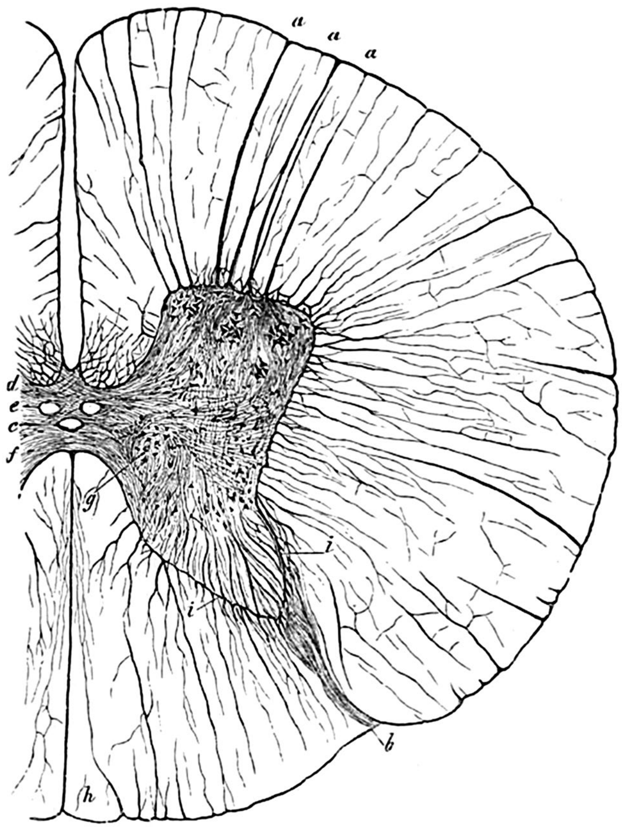


Fig. 10 A drawing of spinal cord section by Koelliker [38], Clarke'sche Säulen oder Stilling'scher Kern (**g**)

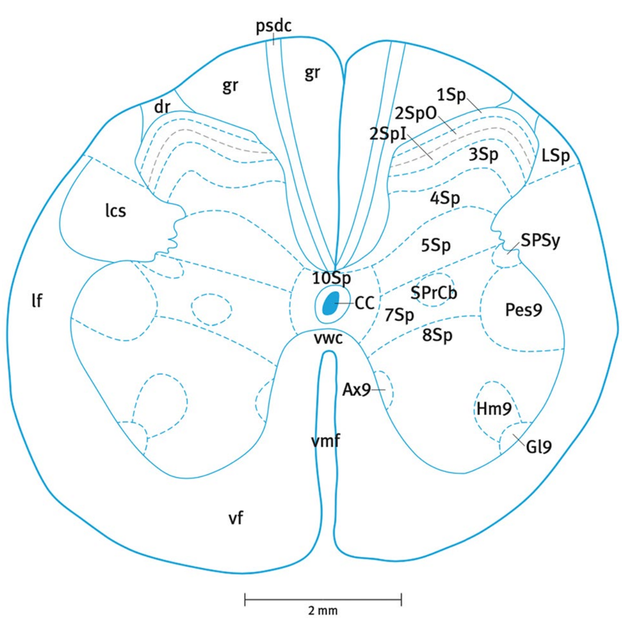


Fig. 11 S1 segment in human spinal cord, prepared by Sengul et al. [34], Stilling's sacral nucleus (SPrCb)

The sacral precerebellar nucleus (Stilling's sacral nucleus) has been shown in the human spinal cord by Sengul et al. in 2013 (Fig. 11) [34]. In addition, in 1984, Molander et al. described the lumbar precerebellar nucleus, which is a cranial extension of the sacral precerebellar nucleus as "the medial group of big neurons in the intermediate zone" in the rat [35, 44, 45]. In 2013, the lumbar precerebellar nucleus in the rat, mouse, marmoset monkey, rhesus monkey, and human has been shown by Sengul et al. [34]. Finally, in 2020, Luo et al. stated that the cerebellum received tail proprioceptive input from Stilling's sacral nucleus in the mouse [46]. It is yet clear that Stilling's nuclei will continue to be an essential subject of spinal cord research, for many years to come.

Conclusion

Benedict Stilling was a pioneer German anatomist and an eminent surgeon. In spite of the fact that Stilling could not acquire an academic career, he was able to contribute substantially to neuroanatomy. We owe numerous developments in neuroanatomy to Stilling, who deserves praise for his diligent work in diverse fields. As a result, he should be remembered as a committed physician and neuroanatomist and be commended for his important works on neuroanatomy.

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Declarations

Conflict of interest The authors declare that there is no conflict of interest.

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