

Magendie and Luschka

Holes in the 4th ventricle

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ABSTRACT. Cerebrospinal fluid (CSF) is a complex liquid formed mainly by the choroid plexuses. After filling the ventricular system where it circulates, CSF flows out to the subarachnoid spaces through openings in the 4th ventricle. Following numerous studies on CSF pathways, these openings were first discovered in the 19th century by two notable researchers, François Magendie and Hubert von Luschka, who described the median and lateral openings subsequently named after them. Even after the studies of Axel Key and Gustav Magnus Retzius confirming these openings, their existence was questioned by many anatomists, yet acknowledged by others. Finally gaining the acceptance of all, recognition of the holes endures to the present day. Interest in these openings may be attributed to the several congenital or acquired pathological conditions that may affect them, usually associated with hydrocephalus. We report some historical aspects of these apertures and their discoverers.

Key words: cerebrospinal fluid, median opening, lateral openings, 4th ventricle, Magendie, Luschka.

MAGENDIE E LUSCHKA: ORIFÍCIOS NO 4º VENTRÍCULO

RESUMO. O líquido cefalorraquidiano é um fluido complexo formado principalmente pelos plexos coróides que, após preencher o sistema ventricular, onde circula, flui para os espaços subaracnóides através de aberturas do 4º ventrículo. Antecedido por numerosos estudos sobre as vias do líquido cefalorraquidiano, estas aberturas foram descobertas pela primeira vez no século XIX graças a dois pesquisadores notáveis, François Magendie e Hubert von Luschka, que descreveram as aberturas mediana e laterais do 4º ventrículo, as quais receberam, então, seus nomes. Apesar dos estudos de Axel Key e Gustav Magnus Retzius que confirmaram a existência de tais aberturas, estas foram postas em dúvida por muitos anatomistas, mas aceitas por outros, para finalmente serem reconhecidas por todos, o que perdura até os presentes dias. O interesse por essas aberturas pode ser atribuído a diversas condições patológicas congênitas ou adquiridas que podem atingi-las, geralmente associadas à hidrocefalia. Aqui são relatados alguns aspectos históricos sobre essas aberturas e seus descobridores.

Palavras-chave: líquido cefalorraquidiano, abertura mediana, aberturas laterais, 4º ventrículo, Magendie, Luschka.

INTRODUCTION

Cerebrospinal fluid (CSF), a complex liquid produced mainly by the choroid plexuses, circulates in the ventricular system, runs out through openings of the 4th ventricle, flows into the subarachnoid spaces, to be finally absorbed mostly at the arachnoid granulations in the superior sagittal venous sinus. The discovery of these openings in the 4th ventricle, first described in the 19th century by François Magendie and Hubert von Luschka,

resulted from continued and tenacious research on the subject.^{1,2} These openings aroused interest for their importance under normal conditions, and in several congenital or acquired pathological disorders, usually associated with hydrocephalus, which may affect them. These conditions include occlusion, membrane obstruction, congenital imperforation, idiopathic stenosis, arachnoid adhesions and cystic dilation, and hamper the normal flow of cerebrospinal fluid.¹

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In this article, some historical aspects of these apertures and the individuals involved in their discovery will be described.

MAGENDIE

François Magendie (1783-1855) (Figure 1) was a French physician, anatomist and physiologist. Among his numerous studies, those on the CSF were impressive, the first of which was published in 1825. In his book “Physiological dissertation on the cerebrum” (*Mémoire physiologique sur le cerveau*) (1828) he recognized the existence of a liquid inside the cranium and spine he denominated, what he called “his” liquid, the “cerebrospinal or cerebro-rachidian fluid” (*liquide céphalo-spinal* or *céphalo-rachidien*).^{3,4,7} Later, in another book, “Physiological and clinical investigations about the cerebro-rachidian or cerebrospinal fluid” (*Recherches physiologiques et cliniques sur le liquide céphalo-rachidien ou cérébro-spinal*), with an accompanying atlas (1842), he detailed observations about cerebrospinal fluid, the ventricular system, the subarachnoid spaces, and the opening he discovered communicating these compartments. Also, he performed experimental procedures to study the dynamics of the fluid (Box).^{3,5,6}

Magendie's median opening. Magendie proposed that the fluid present in the subarachnoid spaces and within the ventricles might be the same, writing: “It is understood that, to confirm such conjecture, it would be necessary that an opening existed to establish a communication between the exterior of the organ [brain] and its interior cavities, and such an opening was yet not known”, and proceeded: “...indeed, after some more research...I finally found an opening...hidden completely by a lobe of the cerebellum, constituting a true entrance of the cerebral cavities”.⁴ He considered the opening remarkable for the direct communication it established between the subarachnoid and ventricular liquids, the location of which he described as follows: “...the constant and normal true opening through which the fluid passes continuously, either to enter the ventricles, or to come out...is seen at the inferior end of the fourth ventricle, near the region named ‘beak of the pen (feather)’ [*calamus scriptorius*] by the ancient anatomists” (*...la véritable ouverture constante et normale par laquelle passe le liquide céphalo-rachidien constamment, soit pour entrer dans les ventricules, soit pour en sortir...elle se voit à la terminaison inférieure du quatrième ventricule, à l'endroit nommé le bec de la plume par les anatomistes anciens*). He named this aperture “opening of the encephalic cavities” (*orifice des cavités encéphaliques*). Magendie described



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Figure 1. François Magendie – portrait by unknown artist (1822).



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https://commons.wikimedia.org/wiki/File:Hubert_von_Luschka_Gem%C3%A4lde_von_M._M%C3%BCller-Sch%C3%BCppel_1896.png

Figure 2. Hubert von Luschka – painting by M. Müller-Schüppel (1896).

how to find the opening, its boundaries, and its variable form and size, but illustrated it poorly in a sagittal section of the cerebrospinal axis (Plate 2, Figure 2-b).^{5,6}

Thus, for the first time, he had uncovered the existence of a median opening of the 4th ventricle that placed this cavity in communication with the subarachnoid spaces, and that was later named after him.^{7,8}

LUSCHKA

Hubert von Luschka (1820-1875) (Figure 2) was a German anatomist. In his book “The choroid plexuses of the human brain” (*Die Adergeflechte des menschlichen Gehirns*) (1855), he thoroughly described the cerebral ventricles, subarachnoid spaces, CSF, and the choroid plexuses. He also applied experimental techniques in order to determine dynamic aspects of the fluid (Box).⁸

Luschka's lateral openings and more. He gave special significance to the 4th ventricle as a gateway linking the other cerebral cavities with the subarachnoid spaces. He described the boundaries, walls, and angles of the

4th ventricle. According to his report, the inferior part of the lateral wall included the external (lateral) angle [lateral recess] [recessus lateralis, Reichert], on each side, as follows: “The external angle thus bounded extends outwards as a channel (duct), through which protrudes the lateral part of the choroid plexus of the fourth ventricle, while the arachnoid is freely stretched over this location. The external angle places the fourth ventricle in open communication with the subarachnoid space. The opening, where the pia mater merges with the ependymal lining, is walled in such a way by the lateral part of the choroid plexus that only a narrow cleft remains... entirely sufficient to allow a liquid...to emerge...” (*Der so begrenzte äussere Winkel verläuft als eine Rinne nach aussen, durch welche der seitliche Theil des Adergeflechtes der vierten Hirnhöhle heraustritt, während die Arachnoidea über diese Stelle frei hinweggespannt ist. Der äussere Winkel setzt daher den vierten Ventrikel mit dem Subarachnoidealraum in einen offenen Verband. Die Lücke, an welcher die Pia mater in das Ependyma übergeht, ist inzwischen durch den seitlichen Theil des vierten Adergeflechtes so verlegt, dass nur eine enge Spalte übrig bleibt...völlig genügt, um Flüssigkeit...Vorscheine kommen zu lassen*).⁸ He also examined the inferior part of the roof, including the inferior angle of the 4th ventricle, and described: “In the inferior tela choroidea there is an elongated rounded...hole, as first identified by Magendie, which provides the main communication of the brain cavities with the subarachnoid space” (*In der untern Gefäßplatte befindet sich eine länglichrunde... zuerst von Magendie näher gewürdigte Lücke, welche den hauptsächlichsten Verband der Hirnhöhlen mit dem Subarachnoidealraum vermittelt*). He thus identified the median opening, and acknowledged that Magendie was the first to find and describe an aperture there.⁸ Luschka accurately depicted the median opening (Plate III, Fig. 1-a), but failed to illustrate the lateral ones he so clearly described, representing only (Plate III, Fig. 3) the inferior surface of the cerebellum, where the choroid plexus, comprising its lateral parts, is displayed.⁸

Thus, Luschka described the lateral openings for the first time, a centerpiece of his research and later named after him, and ratified the existence of the median aperture named after Magendie.^{8,9}

COMMENTARIES

After a very long period of studies on CSF and its pathways, the openings of the 4th ventricle, which communicate with the two compartments (ventricular and subarachnoid), were discovered thanks to Magendie (median) and Luschka (lateral) and later named after

Box. The experimental findings of Magendie, Luschka, and Key & Retzius.

Magendie performed several experiments with human cadavers in order to understand the flow of the CSF, with the injection of aqueous or other liquids through the spinal subarachnoid space, and also by postural drainage. He observed that the liquids never failed to reach the lateral ventricles, and the route, as he stated, was well known – it entered initially through the median aperture, into the 4th ventricle, then passed through the Sylvian aqueduct to reach the 3rd ventricle, and finally the lateral ventricles. Another type of observation was made by emptying the fluid spaces via an opening in the lumbar sac, thus observing the outflow of CSF occupying the subarachnoid spaces. The liquid subsequently flowed from the lateral ventricles to the 3rd, and through the Sylvian aqueduct to the 4th ventricle, to finally escape through the median opening to reach the membranous rachidian sac.^{4,5}

These experiments demonstrated a bidirectional flow of the CSF, and that the median opening in the roof of the 4th ventricle, the only one known at the time, was essential in this dynamic.

Luschka performed seven types of experiments with human cadavers in order to clarify controversial points about the communications of the subarachnoid spaces with each another and with the brain cavities, by applying injections of liquid stained with black ink, or of air, into the subarachnoid space, at several levels, and also by postural drainage. He thus observed that the subarachnoid spaces were in open communication throughout, and that they also communicated with the brain ventricles.⁸ These experiments demonstrated that the subarachnoid spaces remained in free communication with one another and with the ventricles, seemingly in a bidirectional way. However, he was not able to show specific directional flow through the median and lateral openings.

Key and Retzius validated the existence of the openings that permitted communication between the subarachnoid spaces and the ventricular cavities by means of experiments on human cadavers. Into the CSF spaces, they injected solidifying liquids comprising adhesive solutions dyed with soluble Berlin blue (*Berlinerblau*) and molten paraffin mixed with olive oil (*Baumöl*). The injected cadaver was then submitted to refrigeration until it hardened (solidified, set), and only then the brain was removed for study, thus avoiding leaks or displacement due to handling. The median (Magendie's) and the lateral (Luschka's) openings were thus revealed under normal conditions, either after injections into the subarachnoid spaces or into the ventricles. The median aperture was apparently adapted to favor outflow from the 4th ventricle, although the liquid could flow easily into this cavity through this aperture. The lateral openings, on the other hand, allowed the flow of the liquid from within the 4th ventricle to the outside, possibly the main route, rather than from outside into the ventricle, explained by a kind of valvular mechanism, considering that in the presence of stronger pressure acting from outside, the plexus might be pressed against the border of the wall, narrowing or even closing the opening. Thus, the liquid exits the 4th ventricle through the lateral apertures and then flows into the subarachnoid spaces, even with an open median foramen. According to the authors, it was challenging to infer with certainty the direction of the flow through these apertures by means of injections, given that this flow (represented by the hardened material) is found in the ventricle, openings and subarachnoid space, in an uninterrupted stream.¹⁰

These experiments demonstrated the communication of the subarachnoid spaces with the ventricular system, and the perviousness of the median and lateral apertures. The bidirectionality of the median aperture (Magendie's) was ascertained. The directionality of the lateral apertures (Luschka's) was assumed to be from inside out, with a valvular mechanism, but uncertainty remained.

them. It should be pointed out, however, that previous studies on the CSF pathways, some cited below, paved the way for these researchers to achieve their accomplishments.

Axel Key (1832-1901) and Gustav Magnus Retzius (1842-1919),¹⁰ in a review on history they presented in volume 1 of their book “Studies on the Anatomy of the Nervous System and the Connective Tissue” (*Studien in der Anatomie des Nervensystems und des Bindegewebes*) (1875) recalled that suppositions about passages between the ventricles and the subarachnoid spaces were not envisaged before the studies of von Haller, who described (1747) a space between the pia-mater and the arachnoid membrane, and a fluid on the surface of the brain, considering that such specifics were hitherto unknown. He hypothesized that the ventricular fluid (vapor, liquid) must have a route outwards but without offering any substantiation.¹⁰⁻¹² However, credit must go to Cotugno for the first adequate account of the liquid (1764) present in the ventricles and surrounding the brain and spinal cord, and that could mingle at the level of the fourth ventricle, without providing further details.^{10,13,14} Bichat described (1799) a distinct channel ending in the third ventricle, located in the tissue around Galen’s vein, and establishing a communication between the ventricular serous (arachnoid) membrane and the (external) arachnoid membrane, for the liquid to circulate, claiming anatomic and physiologic evidence.¹⁵ However, Magendie, and later Key and Retzius, refuted Bichat’s findings, considering them artifactual.^{5,10} The issue was settled with Magendie’s clear description (1828, 1842) of the subarachnoid spaces (previously reported by Cotugno), and his discovery of a median opening in the roof of the 4th ventricle providing communication of the ventricular with the subarachnoid liquid.^{4,5,8} Later, Luschka completed understanding on the subject, discovering the lateral apertures of the 4th ventricle, related to the lateral recesses and the protruding parts of the choroid plexus (1855).⁸

The investigations of Key and Retzius¹⁰ meticulously described the issue (1875). They confirmed Magendie’s and Luschka’s findings with thorough anatomical descriptions and dynamic experiments, by means of subarachnoid and ventricular injections to demonstrate the perviousness of these openings (Box). They proposed a denomination for the openings – *Apertura inferior* (for the median opening) and *Aperturæ lateralis*

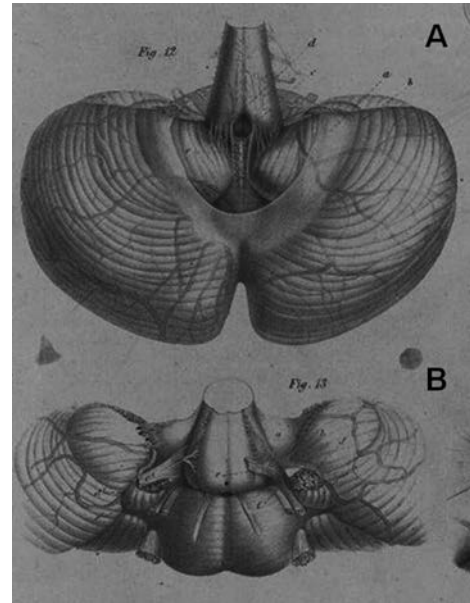


Figure 3. Figures taken from Key and Retzius’s Plate III¹⁰. [A] Figure 12. Cerebellum with medulla oblongata and pons: the medulla oblongata is raised and the arachnoid cutaway in the middle with part of it remaining (a), exposing the cisterna magna and the *Apertura inferior ventriculi quarti* (Magendie’s opening) (d). [B] Figure 13. Medulla oblongata and pons, and the adjacent part of the cerebellum together with the inferior wall of the 4th ventricle. The vermis was cut across, and both lateral halves of the cerebellum bent forward to demonstrate the *Aperturæ laterales ventriculi quarti* (Luschka’s openings). To the right side, the inferior wall of the 4th ventricle (a) with its anterior border (b) can be seen. Between the anterior border and the protruding part of the plexus (d), the *Apertura lateralis* [not labeled] is visible, exposed in full with the glossopharyngeal and vagus nerves (e) folded to the side. The left side shows the natural position of the nerves, almost completely covering the opening.

ventriculi quarti (for the lateral openings), acknowledging the naming after Magendie (according to Luschka) for the median aperture, but maintaining the technical rather than the eponymic denomination for the lateral apertures, and also provided unambiguous illustrations of these openings (Plate III, Figures 12 and 13)¹⁰ (Figure 3). The clear-cut scientific documentation of the main features of the CSF pathways presented, where the openings in the 4th ventricle play an essential role, have remained valid to the present day.^{10,16} Even after confirmatory studies, the existence of these openings was questioned by several anatomists, despite the acknowledgement of many others. Finally, the existence of these openings (holes) was accepted by all researchers, recognition that endures to the present day.¹⁷

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