Humphrey Ridley (1653–1708): 17th century evolution in neuroanatomy and selective cerebrovascular injections for cadaver dissection

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Humphrey Ridley, M.D. (1653–1708), is a relatively unknown historical figure, belonging to the postmedieval era of neuroanatomical discovery. He was born in the market town of Mansfield, 14 miles from the county of Nottinghamshire, England. After studying at Merton College, Oxford, he pursued medicine at Leiden University in the Netherlands. In 1688, he was incorporated as an M.D. at Cambridge. Ridley authored the first original treatise in English language on neuroanatomy, The Anatomy of the Brain Containing its Mechanisms and Physiology: Together with Some New Discoveries and Corrections of Ancient and Modern Authors upon that Subject.

Ridley described the venous anatomy of the eponymous circular sinus in connection with the parasellar compartment. His methods were novel, unique, and effective. To appreciate the venous anatomy, he preferred to perform his anatomical dissections on recently executed criminals who had been hanged. These cadavers had considerable venous engorgement, which made the skull base venous anatomy clearer. To enhance the appearance of the cerebral vasculature further, he used tinged wax and quicksilver in the injections. He set up experimental models to answer questions definitively, in proving that the arachnoid mater is a separate meningeal layer. The first description of the subarachnoid cisterns, blood-brain barrier, and the fifth cranial nerve ganglion with its branches are also attributed to Ridley.

This historical vignette revisits Ridley’s life and academic work that influenced neuroscience and neurosurgical understanding in its infancy. It is unfortunate that most of his novel contributions have gone unnoticed and uncited. The authors hope that this article will inform the neurosurgical community of Ridley’s contributions to the field of neurosurgery.

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Key Words • Humphrey Ridley • circular sinus • cadaver dissection • history of medicine • arachnoid mater • cistern • neuroanatomy

In the modern microneurosurgical era, cadaveric dissection holds an important position for aspiring and practicing neurosurgeons, not only to improve the understanding of the surgical anatomy but also as a tool of advancing neurosurgical operative techniques. Professors Yaşargil and Rhoton led the evolution in the understanding of the surgical neuroanatomy in the late 20th century. Although the use of selective colored cerebrovascular injections in cadaver dissections has recently become a routine practice to enhance the cerebral vasculature, it is an old art that was introduced more than 300 years ago.

Humphrey Ridley, M.D. (1653–1708), a British physician in the 17th century, injected mercury and tinged wax into the cerebral veins of freshly executed criminals, taking advantage of the considerable venous engorgement to demonstrate the anatomy of the venous plexus of the skull base. His work is reflected in the naming of the circular sinus the “Ridley sinus.” Despite this, Ridley remains a relatively unknown figure of the postmedieval era of neuroanatomical discovery.

We reviewed the published works on neuroanatomy authored by Ridley to understand his novel contributions to skull base anatomy and to understand the innovative cadaveric dissections and research methods that he used. This historical vignette attempts to describe Ridley’s academic work and his influence on neuroscience and neurosurgical understanding.

Personal Life

Standard search term strategies including PubMed/ Medline or Cochrane databases failed to return articles on the historical contributions of Ridley. The biographical...
Humphrey Ridley authored the first treatise on neuroanatomy and was interested in global human anatomy and pathological system. Although most anatomists of the period were interested in the neurologomical drawings, Ridley was an innovator who introduced that used a catalyst to harden colored liquids.13 He trusted the objectivity of his senses as opposed to the philosophers of his era, who sought knowledge with their eyes shut.

Ridley was perhaps only the third scientist in history to publish a comprehensive treatise on neuroscience after Thomas Willis’ Cerebri Anatom (1664) and Raymond Vieussens’ Neurographia universalis (1685).10,14,22 In the preface of his treatise, Ridley recognized that both Willis and Vieussens were the inspirations for his work on the human brain.

The principles of research Ridley used in the 17th century were both innovative and admirable. He stated that the nature of the human body could be understood only if one put emphasis on the theory of “cause and effect.” He trusted the objectivity of his senses as opposed to the philosophers of his era, who sought knowledge with their eyes shut.

Although he recognized the role of his predecessors in the work on descriptive neuroanatomy, Ridley performed his dissections and experiments with an open mind. When his observations contradicted earlier reports, he made clear notes in his treatise. Ridley concluded his preface by stating, “I have quoted authors, not out of ostentation, but both for their truth and errors, to the end that at the same time we may see it reasonable and convenient to read all they say, we may be rendered cautious how we believe; and to put us in mind that we find some truth in many things done to our hands by those who have gone before, there is reason we should do something for those who are to come after.”16

Selective Cerebrovascular Cadaveric Injections

Seventeenth century Europe was discovering selective cerebrovascular injections, which increased the understanding of the cerebrovascular anatomy and physiology. The initial work of selectively injecting cerebral blood vasculature in humans and animals was done by Thomas Willis, Richard Lower, and Christopher Wren. They invented syringes and connective silver tubings and used a variety of colored injection materials, such as India ink and liquor, leading to the discovery of the circle of Willis.8,11,14 A few years later, Humphrey Ridley started using warm injections. He used mercury and tinged wax to highlight the cerebrovascular anatomy along with liquor. The tinged wax would solidify upon cooling, making the vascular anatomy clearer and manageable during dissections. Eventually in the 19th century, cold injections were introduced that used a catalyst to harden colored liquids.33 Nowadays, colored silicone and latex injections have largely replaced other techniques of injecting cadaveric heads.18

Ridley and His Treatise on Neuroanatomy

Predilection for the Brain

The Renaissance Period holds a vital position in the history of evolution of the study of human anatomy.4,10,20 During this period, many anatomical discoveries were described and were meticulously documented in anatomical drawings.2,4,11,22 Although most anatomists of the era were interested in global human anatomy and pathophysiology, a few held distinct interests in the neurological system. Humphrey Ridley authored the first treatise focused on neuroanatomy published in English language in 1695, titled The Anatomy of the Brain Containing its Mechanisms and Physiology: Together with Some New Discoveries and Corrections of Ancient and Modern Authors upon that Subject (Fig. 1).16 It was illustrated by the famed surgeon, William Cooper (Figs. 2–5).

In the introduction to the treatise, Ridley described his interest in the human brain: “And this part, I take to be the brain; the delicacy of whole structure is such, that with no little resemblance to its divine author, while it gives us the greatest and the clearest discoveries of other things, lies most concealed itself.”16

Research Motives and Principles

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Ridley developed innovative and effective methods of tissue dissection. In the preface of his book while describing the methods, he stated, “Some of [the cadavers] have been upon subjects in their natural, some in their morbid, some upon those of untimely death; and on those last sometimes whilst the natural fluids remained in their proper vessels, though after a preternatural manner occasioned by strangulation; sometimes when in the room thereof, other bodies have been introduced by injection, as tinged wax and mercury, the first of which by its consistence chiefly, the other by its permanent nature and color, contribute mightily towards bringing to view the most minute ramifications of vessels, and secret recesses of Nature.”

Ridley and the Evolution in Cerebrovascular Arterial Anatomy

Ridley recognized the work of Thomas Willis on the circle of Willis as a masterpiece. He confirmed Willis’ anastomotic principle by selective injections to the carotid and vertebral arteries. He affirmed, “…if even three of the four great arteries [of the circle of Willis] which furnish this part with blood, were totally obstructed, there would yet be a way left for a competent supply from the other unobstructed fourth.”

Ridley pointed out that Dr. Willis failed to show the origin of meningeal arteries from the intracranial internal carotid artery. While describing Willis’ observation and illustration, he stated, “…the very styliform process, where the carotid artery does indeed enter the long canal, to the place where it perforates the Dura Mater to enter the brain, there is not one branch sent out from it; which error, by injecting with wax, which keeps longer in and shows the vessels much better than small tinged Liquors, had very easily been avoided.” He then continued to describe the intracranial origin and distribution of the meningeal arteries.

There is a cursory mention about the labyrinthine artery or the internal auditory artery. While discussing the arteries to the dura mater, Ridley noted, “…and the eight pair of nerves pass out of the Cranium, which passage of this artery is not hitherto described by any that I know of.”

Similarly, Ridley described the ophthalmic artery while discussing the precise origins of the branches of the carotid artery. There is no recorded description of this artery before his treatise. He may have been the first to describe the ophthalmic artery. He described, “One more
branch I take leave to mention only upon the score of its never hitherto having been taken notice of by any, and that’s a small artery attended with a vein passing through the lateral part of the Os Cuneiforme, (which constitutes the back part of the orbit of the eye), just under a very little process of that bone, (which either by reason of its size has escaped being seen, or inconsiderable use, was never before, as far as I know, thought worth the mentioning); and this, upon raising the fore lobes of the brain, offers itself to the eye of any needful observer."16

The ophthalmic artery was later described by Johann Gottfried Zinn (1727–1759), Albrecht von Haller (1708–1777), and F. Meyer (1800s), but unfortunately Ridley’s earlier description of the artery and the vein remains unacknowledged.5–7, 21

Ridley’s assessment of interpreting cadaveric observation was brilliant and objective. He observed that the cerebral veins do not run concomitantly with their corresponding arteries, and he recognized this difference from the other parts of the body. He noted, “the carotid [enters] at the fourth hole in the base of the skull and the internal jugular at the eighth.”16 He expressed dissatisfaction with the explanation offered by his contemporaries for this phenomenon: “…that it may receive equal warmth at the top as at the bottom, as being thereby very much assisted in the production of Animal Spirits in an equal proportion all over...”16 Ridley then described his understanding on this matter as, “…if we consider, that if the veins had ascended with the arteries through the holes in the bottom of the cranium, upon all great ebullitions of the blood, the pulsation of the arteries would in that stricture of the vessels made by the bone, of necessity hinder the freedom of its return by the veins, and consequently occasion a stagnation of blood through the whole brain...”16

Interestingly, he also noted an exception to this rule by giving the examples of veins draining the meninges.

Circular Sinus, Cavernous Sinus, and the Petrosal Sinuses

The skull base venous anatomy was uncharted territory until the 17th century. Ridley stated that Fallopian...
Ridley’s contributions to skull base anatomy and neuroscience

was probably the first to describe the existence of superior and inferior petrosal sinuses. Furthermore, he noted that Vieussens described the origin of the superior and inferior petrosal sinuses from the venous plexus of “Receptacula Sella Equine,” known today as the cavernous sinus or more correctly, the parasellar compartment. 16 This was the first mention of the parasellar compartment in the evolution of the skull base anatomy. Surprisingly, the communication of the 2 cavernous sinuses by the intercavernous sinus or the circular sinus was not reported by Vieussens.

Ridley performed selective venous wax injections and found that Vieussens had missed the circular sinus. He stated, “Another I discovered by having first injected the veins with wax running around the Pituitary Gland on its upper side forwardly within a duplicature of the Dura Mater, backwardly within a duplicature of the Dura Mater and Pia Mater, there somewhat loosely; stretched over the sub adjacent gland itself, and laterally, in sort of a canal made up of the Dura Mater above and the carotid artery on each outside of the gland...thereby constituting a cavity communicating with the two aforementioned forward and backward ones, from whence the above mentioned four small sinus’s do descend by a viable continuity, on each side from a little beneath the hinder process of Sella Turcica: and this from its figure may not unfitly be called the circular sinus” 16 (Fig. 3).

Ridley did not identify the cavernous sinus as a separate entity comprising the venous plexus, carotid artery, and cranial nerves. The sinus was characterized as a distinct structure by Vieussens in 1684 and later by Jacques B. Winslow (who coined the term “cavernous sinus”) in 1732. Winslow elaborated on the trabeculated appearance of the venous plexus apart from the presence of the carotid artery and the course of cranial nerves within the sinus. 12, 23, 24 Ridley considered the venous complex of the cavernous sinus and the intercavernous sinus a single identity of the circular sinus and therefore concluded that the superior and the inferior petrosal sinuses drained the venous blood from the circular sinus complex to the transverse sinus or sigmoid sinus. The rationale behind rejecting the term “receptacle” was that despite the selective injections to the vessels of skull base, he did not find evidence of direct communication between the arterial and the venous anatomy of the “receptacle complex.” Furthermore, he observed that most cranial nerves crossed the posterior fossa to their respective foramina through a duplication of the dura mater and hence could not be described as a part of the receptacle, as described by Vieussens.

Ridley was the first to accurately describe the ganglion of the fifth cranial nerve and correctly identify its 3 branches (Fig. 3) as opposed to 2 branches described by Vieussens. This observation was independently confirmed by Jacques B. Winslow who named the fifth cranial nerve the “nerf trijmeaux,” or trigeminal nerve, in 1732. 24

Ridley and 17th Century Experimental and Translational Research

Arachnoid Layer and the Cisterns

The 2 neuroanatomical identities left unexplored by the artistic medieval anatomists were the cavernous sinus and the arachnoid layer. Until the 17th century, the brain was known to have 2 coverings, namely the dura mater and the pia mater. 19 The first mention about the possibility of a layer separating the 2 meningeal layers was in 1664.
by a Dutch anatomist, Gerardus Blasius (1626–1692).\textsuperscript{19,26} Sanan and van Loveren\textsuperscript{19} reported extensively on the history of the arachnoid membrane. After Blasius, they stated that Frederick Ruysch (1638–1731) was the next to describe the membrane and demonstrate its cobweb appearance by blowing air under it in 1699. In our readings of Ridley’s treatise, it appears that he had empirically described the existence of the membrane before Ruysch.

Ridley mentioned that most of the anatomists, including Willis and Vieuessen, believed that there were only 2 membranous intumegments of the brain. According to him, Govert Bidloo and John Bohn were the 2 anatomists who believed that there was another distinct membrane separating the dura and the pia mater. While testing various cadaveric heads for the arachnoid membrane, Ridley gave an example of an extremely hydroptic brain, in which he clearly appreciated a distinct membrane spanning the brain. He noted that he could successfully divide the membrane easily, especially over the superficial plicatures (folds) of the cortical parts of the brain. To describe its constituency, he wrote, “…I have often observed, not in a continuous, but rather retiform contexture, and so, by such as love hard words, or terms of art, may be called after the same name of that membrane investing the crystalline Humor of the eye, Arachnoeides.”\textsuperscript{16}

He further described that the membrane invests various cerebral vessels and intracranial nerves. Also, he noted, “…there was any larger than ordinary duplicature of this membrane, as there are at the end of Calamus Scriptorius, between the superincumbent Cerebellum and Medulla Spinalis, in the isthmus or space between the Cerebrum and Cerebellum, upon the processes called Nates and Testes…and the first appearance or coming out of the Olfactory nerves…there was found a great deal of water distending this duplicature much beyond its natural limits…”\textsuperscript{16} He clearly pointed out the existence of what we know today as the cerebellomedullary cistern, the quadrigeminal cistern, and the olfactory cistern. Until now, it was thought that the concept of cistern was described for the first time by Bichat in 1802 and François Magendie in 1822.\textsuperscript{26}

Despite Ridley’s descriptions of the cisterns and arachnoid membrane in the 17th century, we do not find any mention of him in the literature with regard to his pivotal work in this area.

**Translational Research**

Rengachary et al.,\textsuperscript{14} while listing remarkable contributions of Thomas Willis, pointed out the nature of some of the experiments done by him on animals, which could be translated to humans. In essence, since his research principles typically demonstrated a “bench to bedside” result–oriented pattern, they advocated that Willis should be considered as a pioneer of translational research.

We found a similar spirit of experimentation and its application to human anatomy in Ridley. He mentioned in chapter 6 of his treatise that numerous anatomists, including Willis and Vieuessen, believed that some cerebral arteries terminated directly into the major venous sinuses of the brain.\textsuperscript{16} Ridley was eager to put this controversy to an end.

He described his experiment: “I took off the upper part of the skull of a dog alive, by which means the Dura Mater with its third Longitudinal Sinus lay bare to the eye and touch, to neither of which senses, at first, either any beating of the membrane in general, or of the Sinus, was the least discernible. After some pause, by chance the Sinus itself, which I designed to have opened with a Lancet, being touched with a cautering Iron, poured out the blood very violently and at first without any remarkable pulsation…I cut this Sinus through almost the length of it, to see whether any arteries would discover themselves by throwing out their salient blood, but no such sign appeared.”\textsuperscript{16}

**Concept of Blood-Brain Barrier**

Ridley’s contribution toward our understanding of blood-brain barrier was recently discussed by Shane A. Liddelow.\textsuperscript{9} Until Ridley, it was considered that the choroid plexus responsible for production and secretion of CSF was restricted to the lateral ventricles. Ridley added to this understanding by describing the presence of the choroid plexus in the third and the fourth ventricles. Moreover, he was the first to point out the differential permeability of the cerebral blood vessels toward a substance (wax/mercury) injected into the bloodstream.\textsuperscript{9,16}

**Other Contributions to Neuroscience**

Ridley was the first to describe a pineal tumor. In chapter 10 of his treatise where he described the “Glantula Pinalis,” he stated, “In an hydroptic Brain of a stumous Boy, I have seen it swelled to a size of three times its ordinary magnitude, and by reason of the abundance of stagnate gelatinous Lympha contained in it, perfectly transparent.”\textsuperscript{16}

Ridley expressed great understanding of the various deep nuclei of the brain in his treatise. Even his description of the fornix and its pathways are regarded to be the first accurate descriptions (Fig. 5).

Ridley made many advances in the art and science of neuroanatomy and neuroscience. These advances are clearly illustrated in his treatises and in his extensive body of work on these topics. Some instances, such as his discovery and descriptions of the ophthalmic artery, the trigeminal ganglion, the arachnoid membranes, and arachnoid cisterns, are very significant in retrospect. Despite these discoveries, his contributions have remained in relative obscurity. We speculate that the reason for his relative obscurity was the nature of clinical and experimental practice. There are no records that reveal his legacy in training a successful generation of leading neuroanatomists or physicians. Additionally, Ridley remained at one institution with minimal contact with outside academicians. Unlike him, his better-known contemporaries, such as Joseph Guichard Duverney, William Cheselden, and Johann Friedrich Meckel, traveled extensively and were keenly interested in training generations of successful physicians and scientists. We can only guess at the stoic nature of his personality. Very little is known about his personal life, and by extrapolation one may assume that he was as private and humble about his work as well.
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Conclusions

Even today, the selective cadaveric injection is considered an art. Humphrey Ridley mastered the art in the 17th century. Through his meticulous cadaveric dissections and experimental research methodologies, he fueled a better understanding of the skull base. His contributions to neuroscience have laid the foundation for modern neurosurgery. Ridley was clearly a pioneer in describing the venous anatomy of the skull base and in providing an accurate description of the fifth cranial nerve ganglion and its branches. He also proved the existence of the arachnoid mater as a separate layer, and he introduced the concept of the subarachnoid cisterns and that of blood-brain barrier. It is unfortunate that most of his novel contributions have gone unnoticed and uncited, but we hope that this article will bring to notice his novel work on brain and inspire the future generation of neurosurgeons to bring innovations to our field.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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