

The Neuroanatomy of Herophilus

J.M.S. Pearce

Emeritus Consultant Neurologist, Department of Neurology, Hull Royal Infirmary, Hull, UK

Key Words

Herophilus · ‘Father of anatomy’ · Galen · Torcular · Calamus scriptorius · Cerebral ventricles

Abstract

Herophilus (ca. 330 to ca. 260 BC) was one of Hellenistic Alexandria’s renowned scholars, a leading physician, often named the ‘Father of Anatomy’. From cadaveric dissections and possibly vivisection Herophilus considered the ventricles to be the seat of the soul, intelligence and mental functions. Herophilus introduced the term *rete mirabile* found in ungulates but not in man, as opposed to Galen, who erroneously believed it a vital human network. A founder of the principles of observations in science, and an exponent of measurements in medicine, his accurate dissections resulted in original anatomical discoveries. He distinguished nerves that produce voluntary motion from blood vessels, and motor from sensory nerves; the nerves of the spinal cord were directly linked to the brain. He identified at least seven pairs of cranial nerves. Herophilus demonstrated the meninges, and ventricles, regarding the fourth as most important. His name is perpetuated by his accounts of the *calamus scriptorius* and the confluence of venous sinuses the *torcular Herophili*.

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‘When health is absent, wisdom cannot reveal itself, art cannot manifest, strength cannot fight, wealth becomes useless, and intelligence cannot be applied.’

Attributed to Herophilus

Alexandria, founded by Alexander the Great (356–323 BC) and established by the Ptolemaic Pharaohs, was the seat of learning for many famous Greek physicians. Its teachers had access to a library of some 7,000 scrolls, probably the largest collection of any country. Hellenistic Alexandria’s renowned scholars included Erasistratus, and Herophilus (ca. 330 to ca. 260 BC) (fig. 1), a leading anatomist and physician in this period, named by many as the ‘Father of Anatomy’ [1–4].

Unfortunately, Herophilus’s treatises were lost in the fire of 391 AD in the Alexandrian Library [5] where they were housed. Fragments have survived in the works of Galen (130–201 AD), and Caelius Aurelianus (5th century). Our main sources are treatises by Galen [6]. However, the fragility of theories founded on disparate historical records [7] and on possible errors in translation must prompt caution. This account of the neurological advances of Herophilus is based on research in translated primary sources that allows a limited evaluation of his work in a historical context. Outstanding amongst them is the exhaustive scholarship of Von Staden [8].

Born in Chalcedon, Asia Minor, little is known Herophilus’s early life. We know he journeyed to Alexandria [8] to begin his education under Praxagoras of Cos [9], who had added to Aristotelian anatomy by differentiating arteries from veins and who first measured the pulse, us-



Color version available online

Fig. 1. Herophilus with his clepsydra from a painting by Joseph F. Doeve (collection of the Houston Academy of Medicine-Texas Medical Center Library). From Fotolia. <http://holykaw.alltop.com/how-human-experimentation-works>.

ing a water clock (clepsydra, κλεψυδρα), thus pioneering objective measurements in medicine.

Herophilus followed the Hippocratic rationalist or ‘dialectical’ method, as opposed to the school of ‘empiricism’. With his younger contemporary Erasistratus of Ceos (ca. 310–250 BC), he practiced medicine with widespread acclaim in Alexandria during the reign of the first Ptolemaic Pharaohs (Soter and Philadelphus). An almost heroic devotion to the teachings of Hippocrates, which he sought to validate, appears to many scholars significant in his investigations [8, 15].

Corpses were generally considered sources of both physical and God-inflicted pollution (stoutly denied by Hippocrates), hence the traditional Greek taboo that banned human dissection [10]. However, for a period of 40 years, Ptolemaic royal patronage permitted dissection of condemned criminals probably to expand understanding of disease and hence the repute of Alexandria as the foremost site of scholarship. After Alcmaeon (6th century BC), Herophilus was probably the first person to dissect human cadavers, numbering about 600 [5, 11, 12]. Soon after Herophilus and Erasistratus, dissection was abandoned [2] until the mid-16th century. There was therefore little anatomical advance until Vesalius’s *De humani corporis fabrica*, 1543. At Oxford University, human anatomy was not taught until 1624. The Murder Act of 1752 in England finally allowed dissection, but only of executed criminals on public display.

Ethical arguments about vivisection performed by Herophilus and Erasistratus [10] were provided by Tertullian (ca. 160–225 AD), and by Aulus Cornelius Celsus (ca. 25 BC to 45 AD), who in *De medicina* (1st century BC) argued: ‘...diseases, arise in the more internal parts, they hold that no one can apply remedies for these who is ignorant about the parts themselves; hence, it becomes necessary to lay open the bodies of the dead and to scrutinize their viscera and intestines’. However, it is unclear whether Herophilus was culpable, for some authorities doubt the authenticity of Celsus’ claims because vivisection by Herophilus is not mentioned in Galen’s often critical writings [13, 14]. Herophilus’s aim was to demonstrate anatomy and explore the nature of disease by dissections. Galen frequently shows respect for Herophilus’s anatomical descriptions, but these had to wait until the revival of human dissection in the Renaissance for explicit recognition of his anatomical accuracy [8, pp. 140–141].

He believed the primary parts of the human body should be perceptible to the senses, following the principles of the Hippocratic school *On the Nature of Man*, probably the work of Polybus, Hippocrates’ son-in-law. His original well-documented [2, 8, 9, 15] depictions of the duodenum, liver, salivary glands, uterus, cardiac chambers are not repeated here.

Nervous System

Praxagoras, his teacher, from the school of Cos was renowned for his studies of the pulse. Herophilus supported him, maintaining that pulsation was involuntary and the result of the contraction and dilatation of the arteries caused by contraction and dilatation of the heart [14] (VIII, 702K). But, based on his own observation, he opposed Praxagoras’s opinion of the ‘cardiocentric’ dictates of Aristotle. Herophilus stated that the brain not the heart was the seat of the soul. As Galen commented, ‘he places the dominant principle of the soul in the ventricles of the brain’.

This was a return to ‘encephalocentrism’ recorded in the Hippocratic treatise *On the Sacred Disease*. It explains why Herophilus emphasised that the brain related to the physical body [15] through motor and sensory nerves. Underlying much of his philosophy can be seen a separation between faculties of the soul and faculties he attributed to nature, the latter was seen as the domain of the physical body, as distinct from the soul: an issue expounded by Imai [16]. The prevailing notion was that diseases resulted from an imbalance or excess of one of the four humours which impeded the pneuma from reaching the brain.

Herophilus considered the fourth ventricle as the most important; he wrote:

This ventricle must be of considerable size and receive the animal spirits previously compounded by the anterior ventricles; so there must be a passage from them to it... through it only there is a connexion (εμπηψισσ) between the cerebellum and the cerebrum [17].

The brain for Herophilus was the seat of intelligence, motion and sensation, and not just a cooling chamber as propounded by Aristotle [5]. The 'governing principle of the body is to be sought in the brain', he wrote in *On Anatomy* [8, p. 154]. This was a revolutionary idea, derived from tentative indications in the Hippocratic corpus and from Praxagoras. Pneuma, the air or spirit, entered the body and was pumped as the spiritus vitalis by the heart in arteries (which he observed to have thicker coats than veins) to the cerebral ventricles and converted into psychic pneuma or spiritus animalis, which was responsible for producing motion, sensation and thought. Herophilus considered the ventricles, especially the fourth, to be the seat of both soul and mental functions whereas Galen later favoured the brain substance itself. Since the brain was the centre of the nervous system, there must be a passage from it, via the ventricles, into the cerebellum, for the spiritus animalis. The concept at this time was of three mental functions: the sensus communis, i.e. the gathering of all sensory perceptions to produce imagination, second of reasoning, and third of memory.

Herophilus, who introduced the term, correctly found no rete mirabile in human subjects [18, pp. 757–759]. Whereas Galen, who performed no human dissections, concluded from ungulates that the basal network of vessels, the rete mirabile, changed the spiritus vitalis into the spiritus animalis which mediated the brain's functions.

Herophilus identified at least seven pairs of cranial nerves [8, (p. 159, 5)], and importantly taught that the nerves of the spinal cord were directly linked to the brain. He described a groove in the floor of the fourth ventricle as the calamus scriptorius, resembling the grooved Alexandrian reed pens (καλαμοσσ = pen). Herophilus named the layered meninges that he described as chorioid owing to its resemblance to the chorion surrounding the foetus. He gave an account of the cerebral ventricles and of the arachnoid membrane lining the ventricles [19]. He reiterated Aristotle, when appreciating the separate convoluted patterns of cerebellum (παραενκεφαλις [paraencephalis]) and cerebrum [20], although cerebellar form and function were not understood until the 2nd century AD. Herophilus also dissected the eye, describing its four coats and the optic (poros) nerve. Herophilus men-

tioned the different parts of the eye, including the vitreous (glass-like humour). The layer at the back of the eye seemed to him rather like a spider's web. Hence he named it the amphiblestroides (latin retina). His dissections also demonstrated the oculomotor, and also trigeminal, facial, vestibulocochlear and hypoglossal nerves [5, 8].

The confluence of venous sinuses – torcular Herophilii, is named after him:

On the crown of the head the doublings of the meninges meet, converging and conveying the blood to an empty space like a cistern, which he called the wine press (Latin, torcular).

He is believed to be one of the first to differentiate nerves from blood vessels in the production of voluntary motion. Galen in *De usu partium corporis humani lib. XII*, noted:

He rightly recognizes that it is the nervous, not the arterial system which serves to produce voluntary motions. This was a power that Galen related to the soul or vital forces, but Herophilus had discerned that nerves convey neural impulses [2, 20].

Gerard Blasius (1625–1692), in his *Anatome medullae spinalis nervorum* (1666) was to demonstrate the anterior and posterior spinal roots and to demarcate grey and white matter of the cord. Although Charles Bell (1774–1842) [21] and François Magendie (1783–1855), both claimed the discovery that dorsal roots mediate sensation and ventral roots carry motor fibres, but it appears that both Herophilus and Erasistratus had appreciated the separate neural pathways for motor and sensory functions [18, pp. 146–148, 22, 23]. It was later suggested by Rufus of Ephesus (c. 98–117 A.D.) in *De anatomia partium hominis* that both of them knew of the existence of 'two kinds of nerves', that could either induce 'voluntary motion' (prohairesis) or were 'capable of sensation (aisthētika)' [24]. It was Herophilus who said: 'nerves that make voluntary things possible (i.e. movements) have their origin in the cerebrum and spinal marrow' [8]. However, he thought it was the body of the nerves rather than some faculty or medium, such as psychic or kinetic pneuma that caused movement, – a concept criticised later by Galen [8, pp. 256–257].

Discussion

Considering that Herophilus and Erasistratus worked at a time when neurological understanding was primitive [20], it is remarkable how much progress they made in anatomy and physiology of the nervous system. Heroph-

Table 1. Herophilus's neurological discoveries (after Acar et al. [25])

Distinguished nerves which produce voluntary motion from blood vessels
Described meninges and arachnoid
Described dural venous sinuses and torcular Herophili
Distinguished cerebrum from cerebellum
Stated ventricles were site of intellect (cf. Galen)
Brain the origin of cranial and spinal nerves
Described ventricles: the IVth and calamus scriptorius the most important
Described cranial nerves II, III, V, VII, VIII and XII
Distinguished motor from sensory nerves
Described rete mirabile in animals, not man

ilus always insisted on the primacy of observable phenomena, not as an attitude of the sceptics but as a cautious approach to unproved theories. He was thus a pioneer in founding the principles of science. His measurements of

the pulse show a new attempt to quantify medical observations.

Lacking significant instruments for physiological experiment, and partly limited by previous prohibitions for dissection, his Promethean advances are even more impressive. Table 1 shows his original anatomical discoveries that underlie much of modern understanding and surgical practice. He was also no stranger to controversy; he sometimes contradicted both Aristotle's dictates and Galen's later brilliant but almost unchallenged opinions.

Several terms (e.g. calamus scriptorius and torcular Herophili) have been perpetuated. The ethical issues posed by his probable use of vivisection can be explained if not excused, partly by Ptolemaic coercion and by the fact that it was common practice in his time in the quest for new knowledge.

The range and magnitude of his studies justify his title as the Father of Anatomy. Galen said of him:

[Herophilus] 'attained the highest degree of accuracy in things which became known by dissection and he obtained the greater part of his knowledge, not like the majority from irrational animals, but from human beings themselves'.

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