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Rufus of Ephesus: a historical perspective on his contributions to neuroanatomy

Esra Candar[1], İbrahim Demirçubuk[2], Gülgün Şengül[1–3]

[1]*Department of Neuroscience, Institute of Health Sciences, Ege University, Izmir, Türkiye*
[2]*Department of Anatomy, Institute of Health Sciences, Ege University, Izmir, Türkiye*
[3]*Department of Anatomy, School of Medicine, Ege University, Izmir, Türkiye*

Abstract

Rufus of Ephesus (circa 1–2 AD) lived in the ancient city of Ephesus, Izmir Province of Turkey. He made significant contributions to many branches of sciences including neuroanatomy. This historical perspective manuscript focuses mainly on his neuroanatomical contributions. He described several structures, such as the pericranium, meninges, encephalon, parencephalon, varicosities, and the anatomy of the sellar region and the eye. He also coined essential terms in the nervous system such as tunica prima (dura mater), tunica altera (pia mater), spinal marrow (spinal cord), base of brain (brainstem), and choroid tunic (choroid plexus). Because of the limited number of extant works, he is not as well-known as his contemporaries. Yet, Rufus of Ephesus deserves to be recognized to the fullest for his precious and numerous contributions to neuroanatomy.

Keywords: history of science; neuroanatomy; Rufus of Ephesus

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Introduction

Rufus of Ephesus lived between the first and second centuries AD.[1,2] The name of the Rufus comes from the residence in Ephesus, Izmir Province of Turkey. He practiced there and assumably in the medical center in Rome, after education at the Alexandria medical school in Egypt.[3,4] He has worked in several fields, such as anatomy, cardiology, psychiatry, nephrology, and ophthalmology. In addition, he has used botanicals to treat various ailments.[1,2,5,6]

Works of Rufus of Ephesus

Rufus, although he wrote more than a hundred books on several topics, is not as well known as his contemporaries because of the limited number of extant full pieces. For this reason, quotes, fragments, translations, and compilations, besides complete treatises, are especially important for his reputation and reconstruction of his works.[2,4,7,8] His works were published in various languages such as Latin,[9–11] Greek,[12] French (**Figure 1a–f**).[13,14]

Many of his works (**Figure 1f**) were collected, extracted from quotations, and translated into French in *Oeuvres de Rufus d'Ephèse* by Charles Daremberg and Emille Ruelle in 1879. Galen (130–200 AD), Oribasius (326–403 AD), Aetius of Amida (500–550 AD), Alexander of Tralles (525–605 AD), Abu Bakr Muhammad ibn Zakaria Razi (865–925 AD) quoted the works of Rufus. Aside from the names included in this book, Rufus was cited by numerous authors such as Avicenna (980–1037), Gilbertus Anglicus (1180–1250), Ibn el Baitar (1197–1248), and Ibn Abi Usaybiah (1203–1270).[2,7,14,15] Indeed, these indicate that Rufus of Ephesus left his mark on many cultures and geographies through the centuries.

The first anatomical terminology pioneering work is thought to be his' work *On the Names of the Parts of the Human Body*.[9,10,12,14,16] English names of his well-known books are *On Kidneys and Bladder Diseases*,[10–12,14] *On Satyriasis and Gonorrhoea*, *On the Interrogation of the Patient*,[14] *Treatise on Pulses*,[13,14] *On Melancholy*,[17] *On Gout*,[14] and *On Icterus*.[18]

Because of his work on *Drug Clearance*,[10–12] he was associated with *"pilulæ Ruffi" (Rufus' pills)* owing to his expertise in pharmacology. He was portrayed with other

Figure 1. Book covers featuring the works of Rufus of Ephesus. (**a**) Latin version;[9] (**b**) Latin version;[10] (**c**) Greek version edited by Jacques Goupyl and Adrien Turnèbe;[12] (**d**) French version of Treatise on Pulses;[13] (**e**) Latin version edited by William Clinch in 1726;[11] (**f**) works of Rufus of Ephesus; a text collated on his manuscripts, translated for the first time into French, with an introduction / publication started by Charles Daremberg, and finished by Emile Ruelle, 1879[14] (Cover pictures reproduced from Public Domain Materials).

medical celebrities in one of the most famous pharmacological and medical manuscripts, *De Materia Medica* (**Figure 2a** and **b**).[19] Pedanius Dioscorides (20–70 AD) wrote *De Materia Medica* (On Medical Matters) in about 65 AD. The illustrated and alphabetical version of this pharmacopeia was accomplished about 512–525 AD in Constantinople (now Istanbul, Turkey). This volume was named *"Juliana Anicia Dioscorides"*, *"Juliana Anicia Codex"* or *"Codex Vindobonensis"*, because it was prepared for Princess Juliana Anicia, daughter of the Emperor of the Western Roman Empire, Anicius Olybrius.[20,21]

Perspectives on Neuroanatomy

The Surgeon Anatomist

Rufus described cerebral berry aneurysms for the first time,[22] and therefore was known as *Magister Chirurgiae*.[21] His surgical skills developed out of his experience in dissection and knowledge of anatomy. He used primates for dissection under culturally restricted circumstances.[23,24] In terms of anatomical features, he selected primates that significantly corresponded to humans, and dissected animals from head to toe *(capite ad calcem)* in parallel with inspection. To compare anatomy with the exterior parts of the body, he used a slave as a human model. He described structures in considerable detail while taking account of his technique and era.[4,25]

Neuroanatomical Contributions of Rufus

Rufus described the brain, the spinal cord, nerves, and ventricles as separate neuroanatomical structures and as parts of a whole, the nervous system.[26,27] Thus, he identified them as connected structures with distinct anatomic components.[28]

He named the bone membrane beneath the scalp *"pericranium"* and defined its junctions, which correspond to the coranal suture *(sutura coronalis)*, sagittal suture *(sutura sagittalis)* and lambdoid suture *(sutura lambdoidea)* in today's terminology.[1,25,29]

Taking an integrated approach to neuroanatomy, Rufus used "osteo-meninges" which is a fundamental oste-

Figure 2. Seven named physicians and botanists of the classical world. Watercolour painting. Early portraits of Greek medical celebrities from a manuscript by Juliana Anicia Dioscorides circa 500 AD, now in the Library of St. Mark's, Venice. (**a**) In the middle: Galen, left with respect Cratevas the botanist, Apollonius Mus, or of Pergamon, Andreas of Carystus; right: Dioscorides, Nikandros of Colophon, and Rufus of Ephesus; (**b**) zoom in on Rufus of Ephesus.[19]

ology term for bones in cavities.[1,25] According to Rufus, the membranes that surround the nervous system are defined as two types of "meninges": the term "encephalitic meninx" for the inner part of the pericranium; and the "dorsal meninx" which is located throughout the back, and the marrow is filled it in.[1,25,30] He mentioned that the spinal marrow descendsed from the encephalon as an extension, making an exit through a foramen in the skull at the occiput, which continued throughout all of the vertebrae.[28] Rufus defined the meninges as robust in two layers with dissimilarity in thickness. The thicker is called *"tunica prima"* which is attached to the bone, and the thinner one is *"tunica altera"* which is adhered to the "encephalon". The terms "dura mater" and "pia mater" were alluded to as earlier synonyms by him.[25,30]

Rufus stated that the brain substance is in ash-gray color, but did not name the gray matter sections of the central nervous system.[30] He described the spinal marrow as an extension of the brain composing of identical constituents.[28] Yet, he did not mention a distinction between the gray matter regions and white matter tracts in the central nervous system. As a synonym for the cerebral gyri in humans, he used the term "varicosities" accounted for the cerebral cortex gray matter.[30] He referred the upper parts of the brain with the term "varicose", and the dorsal and lower parts with the term "base".[1,25,30] His definition of the "base of the brain" is possibly the first indication of the brainstem.[30] He also referred to an extension as the "parencephalon"[1,25] consequently stating an obvious distinction between the cerebrum and the cerebellum.[31]

The first description of the choroid plexus was by Rufus who used the term "choroid tunic".[30] He defined this structure along with the ependyma,[32] which covered the hollows inside the encephalon, and the of *"belly of the brain"* attributed to the ventricles.[25] Rufus was well-informed concerning the ventricular system. He comprehensively clarified the lateral, third and fourth ventricles along with the aqueduct of the midbrain.[23,31] However, Rufus is presumed to cause the misinterpretation that the pia is present in the lateral and third ventricles, but not in the fourth.[30]

Rufus was one of the first to refer to the hypothalamic part of the third ventricle by the term *"infundibulum"*. In addition to this term, he previously used the words the "ditch" and the "hollow". The term *"pelvis"* ("basin", in English language) is referred to by him as the greater part of the hypothalamus, which also contains the infundibulum. The "infundibular stem" was described by Rufus, without knowledge regarding the tuberal part of the anterior lobe.[30]

Due to his particular interest in the sellar region, he examined the neighboring structures of the ventricular system.[23] He was among the first who identified the optic chiasm and agreed on its connection to vision, like his contemporaries Hippocrates, Herophilus, Erasistratus, and Galenus.[23,31] Although Rufus did not give a name, he explained that fibers of the optic nerve crossed in the optic chiasm. He also did some studies on the anatomy of the eye.[30]

Rufus is likely to be the first person who indicated the presence of an anterior chamber in the eyeball.[33] He described the crystalline lens located very close to contact the iris.[5] His descriptions of three ocular membranes are as follows: the first one, called the cornea, is smooth and in the form of a grape. The second choroid membrane is called *"grape-like"* due to its roughness. He named the third arachnoid membrane that surrounds the vitreous as *"crystalline"*. Rufus also cited that Herophilus named the "retina" based on its reticulated form.[25]

Conclusion

Although most of his works are lost, the remaining fragments and quotes reveal Rufus as being ahead of his time. Consequently, Rufus deserves high credit for his unique contributions to neuroanatomy.

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Conflict of Interest

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ORCID ID:
E. Candar 0000-0001-5408-5570;
İ. Demirçubuk 0000-0002-6574-9587;
G. Şengül 0000-0002-5826-7379

Correspondence to: Esra Candar, MSc
Department of Neuroscience, Institute of Health Sciences,
Ege University, Izmir, Turkey
Phone: +90 535 363 15 81
e-mail: esracandar3@gmail.com

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