

History of Neuroscience

Soul, mind, brain: Greek philosophy and the birth of neuroscience

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Abstract

The nature of “soul” and the source of “psychic life”, the anatomical seat of cognitive, motor and sensory functions, and the origin of neural diseases were broadly debated by ancient Greek scientists since the earliest times. Within the space of few centuries, speculation of philosophers and medical thinkers laid the foundations of modern experimental and clinical neuroscience. This review provides a brief history of the leading doctrines on the essence of soul and the properties of mind professed by Greek philosophers and physicians as well as the early attempts to localize brain faculties and to explain neural disorders.

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1. Introduction

Many leading concepts in modern neuroscience find their origin in the speculation of ancient Greek philosophers and physicians. Indeed, questions like the source of human thoughts, the mechanism of cognitive activity, and the nature of emotions, perception and voluntary movement, were disputed by Greek scientists since the beginning of Greek civilization. From the sixth century B.C.E. to the second century A.D., an astounding assortment of conjectures was proposed aimed to unravel crucial issues concerning the essence of soul, the location of intellect and the causes of neurological and psychiatric disorders. In a rational effort to describe and penetrate psychic phenomena, Greek philosophers elaborated theoretical solutions that still fascinate us for their inspired originality and the richness of implications.

The present overview traces the course of the intellectual revolution initiated by some Presocratic philosophers in the sixth century B.C.E. and led to its zenith by Galen in the second century A.D. We shall examine and discuss some leading theories and relevant doctrines in a chronological fashion. What emerges

from this survey is an extraordinary panorama of ideas, which represent the fundamental contribution of Greek philosophy and medicine to the origin and development of the neurosciences (Fig. 1).

An important problem we are faced with is the fragmentary nature of some evidence and the selectivity of the sources. For authors whose work has been largely preserved – like Plato, Aristotle and Galen – we can rely upon entire treatises relative to their written production. For many others, like the Presocratic philosophers or the Hellenistic physicians, available information is not only incomplete but also second-hand. This, of course, raises the obvious problem of the questionable reliability of such information sources because the original opinion may have been misunderstood by the source-author or incompletely reported. The exact nature of the theory professed by a given scholar may be difficult to recover and obscurity must probably remain. Most fragments of Presocratic thinkers, for instance, are preserved as quotations or testimonia from Plato, Aristotle, Theophrastus and Hellenistic sources. Theophrastus’ work, in particular, became the standard source for most subsequent collections of “opinions” (*doxai* or *placita*) on Presocratic philosophy, forming the so-called doxographic tradition [27]. The most important information concerning authors like Diocles, Praxagoras, Herophilus and Erasistratus derives from Galen.

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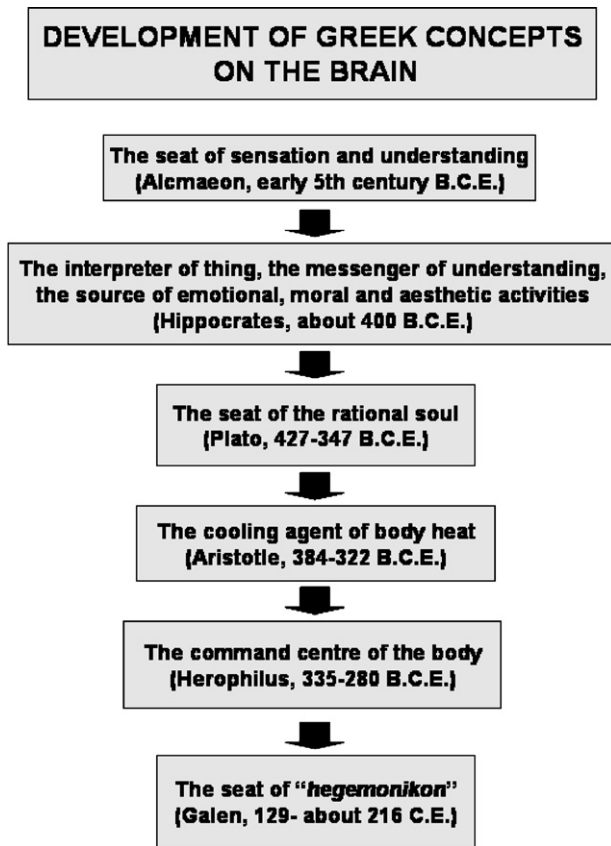


Fig. 1. A schematic box diagram depicting the itinerary of thoughts on the brain elaborated by Greek medical thinkers and philosophers from the fifth century B.C.E. to the second century C.E.

2. The problem of the origin of psychic functions

In Plato's *Phaedo*, Socrates (471–399 B.C.E.) squarely faces the issue of the origin of human thoughts and sketches out with synthetic efficacy the panorama of ideas of former philosophers about the source of men's self-consciousness and cognitive faculties. "And first of all I considered questions like this: . . . if the element by means of which we think is the blood or the air or the fire or nothing of that but rather it is the brain (*enkephalos*) that conveys sensations like hearing, seeing and smelling, so that memory and opinion are produced and, once they had firmly settled [in our mind], knowledge is generated in such way" (96 b)¹ [36].

This passage is of extreme interest for at least three reasons. Firstly, because it raises in a correct way the question as to "what it is in us that thinks"; secondly, because it provides the right explanation insofar as the brain is defined as the locus where human thoughts are elaborated; thirdly, because it establishes that the "substance" which receives sensations is just the same which elaborates them and produces memory, judgement and knowledge.

¹ Numbers and letters between parenthesis refer to citations from the original texts.

This view represented a great scientific achievement but was not shared by all Greek philosophers. In the present contribution, we will first consider the early conception of soul developed in the Greece of Archaic age. Then we deal with the soul and psychic doctrines elaborated in the context of the Presocratic tradition. The early steps of the encephalocentric theory are discussed along with Plato's contribution to the definition of the soul concept. The origin and further development of the cardiocentrism is described later, with particular emphasis on Aristotle's biological philosophy. The great contribution of the Alexandrian anatomists, and the controversy between Stoic doctrines and Galen's epistemology are examined. Finally, a brief survey on the concept of psychic pneuma and the legacy of Greek scientists will be presented.

3. The soul in Homeric times

The Homeric poems were likely composed in the second half of the eighth century B.C.E. but they are representative of an oral tradition reflecting the views of Greeks living in former times. In a celebrated essay on the soul concept in the Greece of Archaic age, the German philologist Bruno Snell put forward the thesis that the Greeks of Homer had not yet developed a unitary concept of the psychic life [40]. Homer distinguished indeed different types of soul. There was a not localized soul – a kind of "life-soul" or "breath-soul" that animates the body, called *psychē* – and different body souls, called *thymos* or *noos* or *menos* [7]. The *psychē* was representative of the individual life and person's identity. This kind of soul was not associated with any specific body part. It was silent during active life but appeared in the dreams during sleeping, left the body during swoons and abandoned the corpse when a person died. At the moment of death, the *psychē* fled away from the limbs or through the wounds and departed to Hades where it began an afterlife. This kind of soul lacked any psychological attribute and possessed merely eschatological traits.

Remarkably, the term *psychē* is etymologically connected with the verb *psychēin*, which means "to blow" or "to breathe". By contrast, the body souls were active during the waking life [7]. The *thymos* was, above all, the source of emotions. It was also the potency that set the body in movement. It resided in the chest, where it was concentrated into the *phrenes*. These were the location of feelings, like joy and grief, pity and revenge, anger and fear. *Phrenes* are generally identified with the diaphragm but some scholars believe that they may also indicate the lungs [33]. The *noos* was more linked with intellectual and rational attitudes. The *noos* intervened when the subject had to reason and ponder. It began to shape the mind concept. It resided in the chest, without any relationship with distinct anatomical structures. *Noos* has the same root of the verb *noēin*, which means "to understand" or "to penetrate". The *menos* was the aggressive impulse, the fury, the rage in the battle. It was located in the chest but was not a physical organ. In Homer's poems we find also the terms *kradiē* or *ētor*, which are translated with "heart". These terms were not related to intellectual functions but designated some source of feelings.

4. Natural philosophers and the Presocratic tradition

During the fifth century B.C.E. a novel, more unitary and abstract idea of soul prevailed in the Greek world. It made its appearance partly as a consequence of the linguistic achievements of the archaic lyrical poets, who developed a new conception of spiritual life [40]. The contribution of natural philosophers to the process of theoretical clarification of the soul concept was relevant. In *Metaphysics*, Aristotle informs us that natural philosophers were a group of innovative thinkers principally interested in explaining the constitution of all matter in terms of specific basic substances [3]. These scholars made the first attempt to interpret natural phenomena rejecting supernatural causes or mythical explanations, and introducing a new critical spirit of rational discussion [28]. These scientists explored different aspects of the physical and biological world and also tried to solve to the problem of the nature of soul. In addition, they faced the question of the relation between psychic activity and the body.

Some of the natural philosophers attributed to distinct physical principles the faculty to elaborate thoughts. Anaximenes (born around 560 B.C.E.), one of the greatest exponents of the Ionian school in Miletus, maintained that the source of human thoughts was the air. Air was the originative substance and basic form of both physical world and psychic life. It was divine and changed by condensation and rarefaction. There was a close relationship between the cosmic air and the breath-soul. One of Anaximenes' fragments so runs: "as our soul, being air holds us together and controls us, so does wind and air enclose the whole world" (DK 2B2) [11].

Of the same opinion was Diogenes of Apollonia (born around 470 B.C.E.), who attributed "thinking and the senses, as also life, to air" (DK 64 A 19) [11]. He held that "the internal air perceives a small part of the essence of god" (DK 64 A 19) [11], implicitly admitting that this element was endowed with intelligence. By contrast Heraclitus (born in the second half of the sixth century), suggested an identification of the rational soul with fire. The world, in his opinion, was an ever living fire. Also human soul was composed of fiery aither and a dry soul was "the wisest and best" (DK 22 B 118) [11], whilst a moistened soul, for example due to excessive drinking, was in an ineffective state. This implicated different states of self-consciousness and cognitive faculties being related to the degrees of fieriness in the soul. Thus, intellect was explicitly placed in the soul.

Other natural thinkers were more interested on the bodily aspects of cognitive processes and argued that the seat of the intellect was localized to specific biological structures or parts of the human body, like blood, chest, diaphragm, heart's cavity, membranes surrounding the heart, head, or brain. Empedocles of Acragas (ca. 495–435 B.C.E.) assigned to the blood, in particular the blood localized all around the heart the function to produce thoughts: "the blood around the heart is men's thought (*noēma*)", he said (DK 31 B 105) [11].

Thus, men think with the blood, and also sensation is a purely physical process. Thinking and perceiving are one and the same process. Empedocles was particularly interested in the mechanism of sensation. He developed the theory of pores

and effluences. Everything is continually giving off effluences, which enter in another body through pores. Sensation is a matter of symmetry of pores. The proper object of each sense fits into the sense-organ.

Parmenides of Elea (born about 515 B.C.E.) also accepted Empedocles' theory of pores and effluences. As to the soul, he localized it to the entire thorax (DK 28 B 45) [11], an opinion later shared by Epicurus (342–270 B.C.E.). Parmenides considered the soul made up of igneous material and regarded it as the human intellect. Democritus (born about 460 B.C.E.), one of the fathers of the atomistic doctrine, maintained that the soul was to be identified with intellect. In his opinion, it consisted of the lightest, fastest moving and spherical atoms with igneous character. Interestingly, he distinguished two parts in human soul: a rational one localized to the chest or the brain, and an irrational one that was "spread over the whole body" (DK 68 B 105) [11].

5. Alcmaeon, Hippocrates and the encephalocentric theory

Since the fifth century B.C.E., two main theories were being worked out by Greek philosophers and physicians to explain the origin of thinking activity: the encephalocentrism and the cardiocentrism (Figs. 2 and 3). The former considered the brain as the seat of human consciousness, sensation and knowledge; the latter attributed all these faculties to the heart. Both theories maintained a passionate and long-lasting controversy within the Greek scientific community, and the dichotomy between

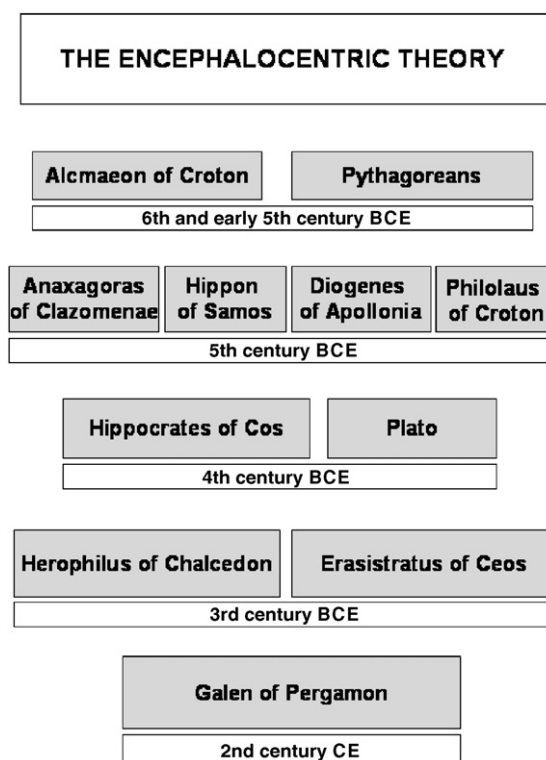


Fig. 2. Box diagram indicating in a chronological fashion the most important Greek exponents of the encephalocentric doctrine.

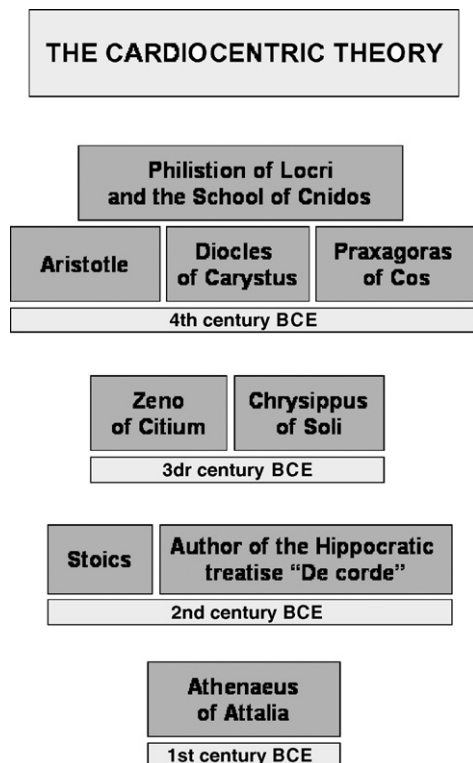


Fig. 3. Box diagram illustrating the most authoritative Greek scholars supporting the cardiocentric view.

encephalocentrists and cardiocentrists continued even in the time of Galen and extended well into Renaissance.

The sensory and cognitive significance of the brain was probably first recognized by Alcmaeon of Croton no later than the early fifth century B.C.E. [29]. He was a physician and, remarkably, made the first anatomical dissections on animal corpses. He stated that “all the senses are connected with the brain” through channel-like structures called “*poroi*”. In particular he described two of such *poroi* joining the eyes to the brain, no doubt the optic nerves. He claimed that the brain was the seat of consciousness and sensation because he recognized that all senses “are compromised if the brain is moved and changes its place” (DK 24 A 5) [11], probably referring to concussions caused by head trauma. Unlike Empedocles, Alcmaeon distinguished between sensation and understanding. Man, says Alcmaeon, differs from the other animals in that he alone has understanding, whereas, they have sensation but do not understand [4]. The word Alcmaeon used to express the concept of “understanding” was “*xynienai*”, which literary means “to put together” [23]: all animals have sensation, but only man can make a synthesis of his sensations. In another testimony, Alcmaeon was credited with the relevant idea that the brain was “the seat, in which the highest, principal power of the soul is located” (DK 24 A 10) [11].

Similar concepts are expressed by other philosophers and biologists of the fifth century. Hippon of Samos localized the principal part of the soul to the head and, in particular, to the brain. Anaxagoras of Clazomenae (ca. 500–428 B.C.E.) and Diogenes of Apollonia recognized that all sensations were connected to the brain.

For the great physician Hippocrates of Cos (about 400 B.C.E.) the human brain resembled that of all other animals, being cleft into two symmetrical halves by a vertical membrane. The Hippocratic Corpus contains outstanding concepts about the brain as the seat of human intellect and the cause of neurological disorders.

In one of the earliest treatises, *De morbo sacro*, we find the most important epistemological claim that epilepsy, called in antiquity “the sacred disease”, is not “any more divine or more sacred than other diseases, but has a natural cause, and its supposed divine origin is due to men’s inexperience and to their wonder at its peculiar character” [26]. The cause of the sacred disease is to be found in the brain, which “has the most power in man. If it is in sound conditions, it is our interpreter of the things . . . The eyes and ears and tongue and hands and feet do whatever the brain determines; for there is an element of intelligence in the whole body . . . , but it is the brain that is the messenger to the understanding” [26].

In another remarkable passage of *De morbo sacro*, the brain was also regarded as the seat of judgment, emotions and aesthetic activity: “our pleasures, joys, laughter and jests arise from no other source than the brain; and so do our pains, grief, anxieties and tears. Through it . . . we also discern ugly and beautiful, bad and good, pleasant and unpleasant” [26]. Thus thinking activity, moral consciousness, perceptive elaboration and control of body’s movement were functions all localized to the brain.

Hippocrates was also credited with the powerful image of human mind being “placed in the brain like a holy statue” (I, 4) [20]. In a psychiatric context, he explained mental insanity as a process of brain corruption induced by bile, one of the four humours (blood, yellow bile, black bile and phlegm) responsible for the states of health and illness.

Remarkably, the Hippocratic canon contains passages dealing with lateralization of the effects of brain injury. In one passage, it was stated that “an incised wound in one temple produces a spasm in the opposite side of the body” [8]. In another relevant passage, it was recognized that loss of speech occurred with “paralysis of the tongue or of the arm and the right side of the body [8]. Despite these outstanding observations, there are no proofs that Greek physicians were aware of the concept that the two cerebral hemispheres would control the opposite sides of the body and, in particular, that aphasia depended on a damage of the left hemisphere that also caused right hemiplegia.

6. The doctrine of soul in Plato

Plato (427–347 B.C.E.) supported the concept of the primacy of the brain as the organ of the rational soul. The most complete formulation of Plato’s theory of human soul (*psychē*) is to be found in *Timaeus*. According to Plato’s view, there are three soul species in the human body. Only the first one was qualified as “immortal” and “divine”, the *logos*. It was called “the imperishable principle of the deathly animal” [34,35]. This soul was recognized to be bound to “the head, which is the most divine part and dominates over the rest [of the body] in us. And the gods gave to this part also the whole body as servant” [34,35]. With this sentence, Plato conferred a hierarchical primacy to the

head over each other part of the body. In a following passage, Plato better specified the anatomical seat of this soul: “one part, like a field, had to receive the divine seed in it, and this part of the marrow moulded [the gods] wholly round and named it brain (*enkephalos*) because . . . the vase that contained it was the head (*kephalē*)” [34,35]. This soul is intelligent, rational but invisible. Thus Plato, following Pythagoras, developed the concept of the body as a temporary receptacle of the immortal soul, which could pass from one body into another at death.

Besides the immortal soul, Plato recognized the existence of two other species of perishable souls. The first one was the source of the feelings, like boldness, fear, anger and hope; it was the *thymos* [34,35]. This irascible part localized to the chest, above the diaphragm and near the heart and lungs. The heart had the task of keeping a watch over it, like a guardian. It was not completely separated by the immortal soul but was connected with this through the isthmus of the neck. “[The gods] made the deathly species [of soul], and in the fear of contaminating the divine . . . they placed the perishable one in another body site, far away from it, and established an isthmus and a boundary between the head and the breast, placing the neck in-between, in order to keep them separated. Thus in the chest and in the so-called trunk they bound the perishable species of soul. And because one part of it had a better character and one worse, they divided the cavity of the trunk in two compartments . . . and placed the diaphragm as a seal in the middle. And they placed that part of the soul, which takes part to bravery and rage and is belligerent, nearer the head, between the diaphragm and the neck because, being subordinate to reason and agreeing with it, this would strongly repress the greed” [34,35]. Remarkably, the word diaphragm made here its first appearance as a technical term in the history of anatomy.

Wholly distinct and physically separated from the former two species was the soul of nourishment, the *epithymētikon*. This “craves for food and drink” [34,35]. The concupiscible soul was situated in the region between the diaphragm and the umbilicus, near the liver, as distant as possible from the deliberating soul. It was the seat of passions, desires and unconscious life, like dreaming and foreboding. It “has neither opinion, nor reasoning, nor intelligence but pleasant and painful sensations” [34,35]. At last, Plato mentioned a fourth species of soul, the soul of sexual impulse. This localized below the umbilicus and was fully irrational and unwilling to accept discipline.

Plato’s tripartite schema of human soul was not entirely original. As mentioned previously, Democritus, roughly contemporary with Plato, distinguished a rational soul related to the chest or the brain, and an irrational soul extended over the whole body. Some essential features of Plato’s tripartite view were derived indeed from Pythagorean speculation [6].

Philolaus of Croton (ca. 470–385 B.C.E.), almost contemporary with Socrates, developed a four-fold system of psychic and vital principles in man. He distinguished the following anatomical structures, each associated with distinct psychophysical aptitudes. The head was conceived as the seat of the intellect; the heart was regarded as the foundation of life and sensation; the umbilicus was interpreted as the source of rooting and embryo’s development; the genital organs were considered the

origin of fertilization as well as generation [31]. A testimony from Diogenes Laertius identifies the origin of the concept of soul partition in the context of early Pythagoreans. According to this testimony, they conceived the human soul as a tripartite structure. The brain was the seat of the mind (*nōus*) and the rational faculty (*phrenes*), whilst the heart was the place of courage, bravery and audacity (*thymos*) (DK 58 B 1a) [11].

7. The heart and the cardiocentric theory

7.1. Aristotle

The notion that the heart was the source of emotions and thoughts was much diffused in the ancient world, in Egypt and Mesopotamia for instance [13]. By the Greeks, it can be traced back to Homeric poems. In Iliad and Odyssey indeed, we find the soul placed either in the *phrenes*, usually the midriff, or in the chest, but sometimes also in the heart [7]. The importance given to the heart as the seat of soul and intellect was likely based upon the anthropologic evidence that life occurred as long as the heart kept pulsating and death supervened after cessation of heart activity. In addition, the heart was associated with the vital heat and, in Empedocles, we have seen that the blood around the heart, which was the most important vehicle of life heat, was indeed the source of human thoughts. The origin of the “scientific” theory assuming the heart as the seat of intelligence and sensation is obscure. It has been ascribed to Sicilian physicians, like Philistion of Locri, and to the School of Cnidos in Asia Minor but this opinion is not accepted by all scholars [24].

It was Aristotle (384–322 B.C.E.), the greatest of classical biologists and probably the first anatomist in the modern sense of this term, who gave a definite and authoritative character to the cardiocentric theory [21] (Fig. 3). According to Aristotle, the soul is defined as the substance or the form of a living body [4]. It is indeed the primary cause of living, perceiving and thinking. He distinguished different soul faculties [4]. The vegetative or nourishing soul belongs to both plants and animals. Sensitive and motor souls pertain only to animal. The intellectual soul (*nōus*) is limited to man. All soul faculties reside in the heart. Only the *nōus* is immaterial. Thus the heart occupies the uppermost place in Aristotle’s psychological and physiological hierarchy. It is regarded as the central organ of the body, the principle of life, the generator of body heat, the font of blood and the origin of vessels [1,2,5]. Accordingly, it is the organ that develops first in the embryo.

Aristotle, however, provided also interesting contributions to brain anatomy. He observed that the brain in all animals was placed in the front portion of the head and was surrounded by two membranes, the meninges, which were patterned with blood vessels. The external envelop, situated next to the bone of the skull, was the thickest (no doubt, the *dura mater*); the internal, localized around the brain itself, was more delicate (probably, the *pia mater* or *pia mater* and *arachnoid*) [1].

As to the brain, this was bloodless, cold and bipartite. Aristotle made for the first time the important anatomical distinction between cerebrum (*enkephalos*, brain) and cerebellum (*parenkephalis*, para-brain) [1]. The latter was positioned

beyond the former, to the back, and its shape and texture were recognized to be different from those of the brain. In addition, Aristotle identified three possible nerves, he called “*poroi*” (“ducts”), two of which – the largest and the second largest – led to the cerebellum, the smallest to the brain itself [1]. It has been suggested that these passages might possibly refer to the optic nerve and tract, and to trigeminal and oculomotor nerves [9,42]. Of course Aristotle had no concept of nerves, and there was for him no nervous system as such. He also recognized a cavity in the brain, a small hollow, probably the ventricular system, and made the interesting observation that Man has the largest brain in proportion of his size. Elsewhere, he referred to “liquidity about the brain” [2], a possible reference to the cerebrospinal fluid. In opposition to Plato’s opinion, he correctly described the spinal cord as an extension of the brain and recognized a similar constitution for both structures [2].

Despite such relevant anatomical contributions, Aristotle’s speculation about brain functions was rather disappointing. In his view, the brain played indeed only a subsidiary role. Being bloodless it had no sensory properties because “the instruments of sensation are the blood-containing parts” [2]. In addition, Aristotle recognized that the brain was insensible when touched. As the moistest and coldest of all the organs, it served merely to diminish the heat of the blood generated by heart [5]. It had therefore no intellectual meaning. Notably, however, Aristotle implicitly assigned to the brain a somewhat ambiguous and indirect role in human consciousness and psychic activity insofar as this organ had the task to temper the excess of vital warmth produced by the heart [9,10]. In this perspective, the brain was regarded as the inductor and generator of sleep [2,5].

7.2. Diocles

Considered by Pliny the Elder one of the most reputable of the ancient physicians, Diocles of Carystus (flourished in the fourth century B.C.E.) reasserted the role of the heart, “the body’s leader from which the psychic pneuma moves to the body” (V, 1) [20], as the physiological centre of sensation and thought. He made progresses in the description of the heart functional anatomy and recognized the two cardiac ears or auricles. This important discovery, however, was misinterpreted in the light of his theory of the cognitive function of the heart. Indeed, he attributed the role of sensory organs to these appendages, through which the heart would always be listening and understanding [42].

Most remarkably, Diocles later modified the doctrine of the cognitive primacy of the heart by suggesting that the right half of the brain provided sensation and the left intelligence, even though the heart remained in his opinion the centre for hearing and understanding [13]. This heart–brain “double seat” theory, with the heart prevailing at last, is well exemplified by a series of fragments reporting Diocles’ view on some psychiatric and neurological diseases. In his opinion, madness was “boiling of the blood in the heart” (XVIII, 2) [20] whilst lethargy was “a chilling of the psychic pneuma about the heart and the brain and a freezing of the blood dwelling in the heart” (II, 2) [20], and

melancholy was considered as a disorder arising “from thickening of black bile around the heart” (XIX, 1) [20].

7.3. Praxagoras and followers

Praxagoras of Cos (born about 340 B.C.E.), the teacher of the great Alexandrian anatomist Herophilus, still ascribed all psychic faculties to the heart and blood vessels. He was credited to be the first who made a general distinction between arteries and veins, recognizing different functions to them. He conjectured that arteries would carry the pneuma and attributed to the only veins the role of transporting the blood. Being a physician, his view on the origin of thought, sensation and movement was strongly influenced by the problems he encountered in his clinical practice. According to him, the cause of madness was to be found in “a swelling of the heart, to which thoughts belong” (XVIII, 1) [20] and delirium (phrenitis) “is inflammation of the heart, whose natural activity he holds to be mental sanity” (I, 2) [20].

Praxagoras held the view that the arteries were the routes through which the pneuma flowed from the sense organs to the heart, and thence to the muscles. Discussing on the origin of epilepsy, he made the remarkable statement that this disease “arises around the thick artery [aorta] from phlegmatic humours that gather in it; by producing bubbles, they stop the passage of the psychic pneuma out from the heart and so this vibrates and produces spasm in the body” (III, 1) [20]. The causes of paralysis and tremor were to be found within the same conceptual framework. In his opinion, the former occurred “because of thick, cold phlegm around the offshoots of the heart and of the thick artery” (XXI, 2) [20], whilst the latter was generically defined as “an affection of the arteries”.

The cardiocentric thesis enjoyed a great success well beyond Aristotle, Diocles and Praxagoras. Among others, it was accepted and supported by the Peripatetic tradition, by Athenaeus of Attalia, the founder of the Pneumatist medical sect (first century B.C.E.), and by all the Stoics. In the Hippocratic treatise *De corde*, a text of controversial date but almost certainly post-Aristotelian, we find the statement that the mind (*gnōmē*) resides in the left ventricle, which rules the rest of the soul [31].

8. The Alexandrian medical school

8.1. Herophilus

In Ptolemaic Alexandria, during the third century B.C.E., flourished a renowned medical school, whose most significant exponents were Herophilus of Chalcedon (335–280 B.C.E.) and Erasistratus of Ceos (310–250 B.C.E.) [30]. It is not certain, however, that Erasistratus lived and worked in Alexandria, although he undoubtedly belonged to the scientific and intellectual Alexandrian milieu [14]. Both practised dissection of the human body, vivisected animals, and probably also criminals sentenced to death. Herophilus, in particular, is considered the founder of human anatomy as a distinct branch of medicine. Some of his pioneering discoveries in almost every field of

human dissection are regarded as the highest medical achievements until the 17th century [15]. Unfortunately, the original writings of these two physicians have gone lost and we must rely upon later references from different sources, in particular Galen.

Herophilus was credited with a series of accurate descriptions of neuroanatomical structures and his brain anatomy largely surpassed the standard of his time. He provided a clear distinction of the brain ventricles, recognizing that they allow passage of the psychic pneuma because they are in reciprocal communication, “and therefore there is an obligatory passage from the front ventricles into the ventricle of the cerebellum” [17]. He gave a particularly precise account of this cerebellar ventricle, the fourth ventricle or the posterior ventricle, to which he attributed great functional significance as the seat of *hegemonikon*, the ruling principle of the body. In addition, he described and nominated some unique structures visible on the floor of this cavity, such as the “*calamus scriptorius*”, the posterior median sulcus and the “*colliculus facialis*” [18]. He accepted Aristotle’s distinction between *enkephalos* and *parenkephalis*, recognizing that they are separated by a thick membrane (*tentorium cerebelli*). He described the tunic covering the ventricles of the brain as the “choroid meninx” and was considered, along with Erasistratus, to be the first anatomist who identified motor and sensory nerves, correctly locating their origin in the brain or in the spine [17]. He gave careful description of at least seven pairs of cranial nerves, among which the optic, oculomotor, trigeminal, motor root of the trigeminal, facial, acoustic and hypoglossal nerves [18].

No less impressive was Herophilus’ physiological interpretation of his anatomical findings. He stated that the fourth ventricle and possibly the overlying cerebellum were the control centre of human motility. In his opinion, “the ventricle in the cerebellum exercises more control” in comparison to the anterior ventricles [17]. Herophilus developed this theory because he found that “all the nerves of the body below the head grow either from cerebellum or from the spinal marrow” [17], which is near to the fourth ventricle. Some scholars maintain that this conjecture derived also from experimental work on vivisectioned animals.

Remarkable was Herophilus’ view of nerve function, which was shared by Erasistratus as well: there are two kinds of nerves, the sensory (*aisthētika neūra*) and the motor nerves (*kinētika neūra*), and “the nerves that make voluntary motion have their origin in the cerebrum and the spinal marrow” [18]. Herophilus’ rational approach to the dissection of the nervous system, his identification of the psychophysical command centre to the region of the hindbrain (the fourth ventricle and the cerebellum), the description of cranial and spinal nerves and the fundamental distinction between sensory and motor nerves were his extraordinary contribution to the development of what much later will become the neurosciences.

8.2. Erasistratus

Younger than Herophilus, Erasistratus was himself a skilful neuroanatomist even if his main contributions were to be found in the field of physiology [31]. He provided a remarkable

description of human brain and cranial nerves, distinguishing nerves for sensation and nerves for movement [19]. He assigned, however, the greatest functional significance to the thick membrane (*pachēia mēnix*) enveloping the brain, the *dura mater*, which he long considered the command seat of sensitive, motor and cognitive functions. As a consequence, psychiatric and neurological disorders were interpreted as depending on pathological changes concerning this structure.

Considering the cause of lethargy, for instance, Erasistratus stated that such dysfunction “arises from an affection of the psychic faculty in the meninx, which is precisely where lethargy occurs” (II, 1) [20]. And the source of delirium was to be found in “a disorder of the activity of the meninx” (I, 1) [20]. Initially, he also described the nerves as anatomical structures, which originated from the meninges. This opinion was apparently supported by the demonstration that experimentally induced lesions of the cervical meninx in the ox caused death of the animal [16]. In addition, he maintained that wounds inferred on the right side of the cerebral meninx determined paralysis of the left body side and vice versa. Such observation was explained by the assumption that the nerves running in the right hemisoma originated from the left side whilst the nerves distributing to the left hemisoma arose from the right side (42 A) [19]. In his old age, probably on account of more accurate dissections, Erasistratus recognized that the nerves originated from the substance of the brain. Outstandingly, he established a relationship between the intelligence of man and the number and complexity of the convolutions of human brain (289) [19].

9. Nerve function and the psychic pneuma

A short review of Greek doctrines on soul and mind cannot get out of a brief discussion on the concept of nerve structure, the theory of sensory perception and the execution of voluntary movements, as they were elaborated by the ancient scholars. Greek scientists conceived of nerves as “ducts” or “channels” or “pathways” (*poroi*) for the passage of the “psychic pneuma” (*psychikon pnēuma*), the light and invisible substance considered to perform sensory, motor and mental activity [41].

The first account of the nerves as hollow structures regards the optic nerve and probably dates back to Alcmaeon of Croton. He described two “ducts” that proceeded down from the brain to the eyes (DK 24 A 10) [11]. The unique perforated structure of the optic nerve, with the central artery of the retina running inside its distal tract, had likely a great impact on the elaboration of a general theory of nerve function. Aristotle, as already mentioned, gave account of three possible nerve structures, he actually called *poroi*, which might have corresponded to the optic nerve and tract, and to trigeminal and oculomotor nerves [1]. Herophilus too called the optic nerves *poroi* and so did Eudemus, a distinguished anatomist contemporary of Herophilus [18].

Thus nerves were conceptualized by Greek scientists as luminal structures carrying the psychic pneuma. This permeated the hollow nerves and flew down from the cerebral ventricles to the sensory organs and to the muscles, performing sensitive functions and voluntary movement. The role attributed to the psychic pneuma can also be inferred by the pathogenic interpretation of

several mental and neural diseases. As a result, the aetiological explanations of disorders of the motor and nervous system were conceived of in keeping with such a model of nerve physiological anatomy. Interestingly, Erasistratus held the view that motor paralysis occurred because “the liquids in the veins transfuse into the cavities of the nerves through which voluntary motions are performed and hinder the faculty, which flows down through the body from the principle” (XXI, 1) [20]. Spasms in the muscles were believed to occur because “the nerves rising from the brain are filled by certain viscous, sticky humours, by knocking against which in passing the psychic pneuma brings about convulsions” (VII, 1) [20]. And apoplexy arises, according to Erasistratus, because “cold, frozen phlegm forms in the brain: the nerves that arise from the brain, filled by this phlegm, do not receive the psychic pneuma” (IV, 2) [20].

The origin of the psychic pneuma was a much debated and controversial subject. Herophilus was probably the first to introduce a new nerve physiology by extending to the nerves the pneumatic mechanism that his teacher Praxagoras had applied to arteries [32]. According to his view, the psychic pneuma was prepared in the front ventricles of the brain and then travelled to the ventricle of the cerebellum, which he considered the body’s command centre [17]. This ventricle “appears large and the passage entering into it from the anterior ventricles is very large indeed” [17]. Then the psychic pneuma enters motor nerves to generate movement. It was Erasistratus, however, who developed an organic and coherent doctrine of pneumatology [39]. He distinguished two types of pneuma: vital and psychic. The inspired air becomes “vital pneuma” as it passes from the lungs to the heart via the pulmonary vein. The psychic pneuma derives from the vital pneuma, which exits from the left cavity of the heart upon heart contraction, runs in the arteries and is distributed to the whole body. Once the vital pneuma reaches the meninges, it passes in the brain ventricles and eventually enters the nerve cavities turning into psychic pneuma (112, 240) [19]. According to Erasistratus indeed, “the beginning of the sensory nerves which are hollow, you could find in the meninges of the brain, and those of the motor nerves in the brain and in the cerebellum” (39) [19]. Later on, Erasistratus’ pneumatic doctrine was refined by Galen, who elaborated a comprehensive and systematic theory of the functions of pneumas [32].

10. Galen and the controversy with the Stoicism

Galen of Pergamon (129 to about 216 C.E.) was one of the greatest physicians and biologists of all times. He lived in a composite spiritual and intellectual atmosphere, the Roman Empire of the second century C.E., which was permeated by different philosophical doctrines and soul beliefs. Galen devoted much experimental and theoretical work to the study of brain functions. He was a convinced assertor of the centrality of brain in elaborating thoughts, sensation and movements, and harshly fought against cardiocentric views sustained by Stoic philosophers. The brain – says Galen – is that part which “receives all sensations, produces images and understands thoughts” [17]. Galen’s encephalocentrism was influenced by the work of a number of earlier scientists, in particular anatomists. He

praised Herophilus, Herophilus’ fellow Eudemus, Numisianus and, above all, Marinus of Alexandria, who flourished about 120 C.E.

Central to Galen’s approach to brain investigation was his belief of the absolute need of a rigorous anatomical methodology. He claimed indeed that only correct dissections would provide “apodeictic proofs”, or incontrovertible demonstrations, which in turn, enable the researcher to draw legitimate conclusions [17]. For him, the brain is the *hegemonikon*, the ruling principle and the regent part of the body. He founded this assertion on a series of specific points. The brain alone is responsible for sensation and voluntary motion, which both are the main attributes of the rational soul [16]. He based his view on the claim that the brain and the spinal cord were the only sources of the nerves, an assertion strongly contrasted by cardiocentrists, who maintained that the heart was the origin of all body nerves.

Indeed, thanks to his rational investigative methodology and first-rate anatomical skill, Galen reached the conclusion that the nerves and the spinal cord were composed of the same substance of the brain [17]. He also provided a clear demonstration that the spinal cord originated from the brain. It is controversial whether Galen had access to dissection of human bodies. If this occurred, it was only occasional and fortuitous because, after the short parenthesis related to the unique intellectual and social environment of third century’s Ptolemaic Alexandria, the Greek reverence and dread of the dead human body had got the upper hand over scientific investigation. For practical purposes, we can conclude that all his anatomical and vivisection brain experiments were performed in animals, in particular the ox, and extrapolated to man. Remarkably, Galen did not attempt to localize the rational soul in a specific part of the brain. In his opinion, it was the psychic pneuma that functioned as the first instrument of the rational soul. Thus the psychic pneuma is the effector agent of the soul. Indeed, all Galen’s physiology of the brain is dependent upon pneuma. It is the psychic pneuma indeed that, in a way Galen failed to explain, accounts for mental activities like thoughts and memory as well as sensation and voluntary motion.

This leads us to consider another crucial point of Galen’s brain epistemology that is the anatomical architecture and the supposed functions of the brain ventricular system. Galen provided a very sophisticated description of the four ventricular structures deeply situated in the brain [17,18]. These communicating cavities function, in Galen’s opinion, as an integrated whole. They are patent spaces, which harbour the psychic pneuma. This moves indeed within the interconnected spaces of the ventricular system, continues through the nerves to the rest of the body and conveys, in an unexplained way, sensation and movement [6]. If nerves are cut, they are no longer able to conduct the psychic pneuma. As a consequence, sensation or movement disappear depending upon sensory or motor nerves are damaged.

On the same ground, Galen claimed that ventricle exposure resulted in loss of motion in the animal. As to the origin of the psychic pneuma, Galen postulated a mechanism that became a biological paradigm in the following 1300 years. In his view, the psychic pneuma was mainly produced by two vascular struc-

tures placed within the anterior and middle ventricles and at the base of the brain, namely the *choroid plexuses* and the *retiform plexus* or *rete mirabile* [16,17]. These specialized networks of fine blood vessels were responsible for the transformation of the vital pneuma into psychic pneuma. It should be noted that Galen's *rete mirabile*, to which he placed so much importance, was not even found in humans and he observed it probably only in the ox and the sheep. Galen admitted, however, that a limited proportion of psychic pneuma would be elaborated from outside air inhaled through nasal passages.

Stoics were among Galen's most formidable adversaries. All the Stoics indeed maintained that the soul and the intellect were situated in the heart or in the pneuma around the heart [28]. They also established a strict relationship between the human microcosm and the physical macrocosm. The heart was the sun of human life and thus it was regarded as the seat of the *logos*, the universal intelligence [31]. Galen had much to fight experimentally and theoretically against these cardiocentric assumptions. He maintained that Stoics' assertions were false because they relied upon poor experimental methodology and because they were rhetorical. Stoics indeed founded their arguments on weak bases, like common opinion, authority of poets or word etymology. For instance, the early Stoic philosophers Zeno of Citium (331–262 B.C.E.) and Chrysippus of Soli (277–204 B.C.E.) claimed that the heart was the place of *hegemonikon* because the human voice, in their opinion, was generated by the heart. Against such rhetorical arguments, Galen opposed a series of logical confutations based on rigorous and objective anatomical demonstrations. He gave proof, for instance, for the disappearance of the voice after incision of the inferior laryngeal nerves in the pig and other animals [17]. According to Gross, this may have been the first experimental evidence that the brain controls behaviour and thought [22]. In addition, Galen rejected Stoics' cardiocentric assumptions on the ground that the heart produced neither sensation nor modification of consciousness when touched [16].

11. Concluding remarks

This is a survey of the contribution of Greek philosophy and medicine to the development of original concepts about the nature of soul, the faculties of mind, and the structure and function of the brain. At the end of this study we wish to single out three issues, which in our opinion, represent the greatest achievements transmitted by Greek thinkers to later generations of neuroscientists.

Firstly, Hippocrates' conception of human brain. As early as the fifth century B.C.E., this pioneer physician had already worked out an astounding and absolutely modern view of brain functions. Indeed, the brain was not only considered the seat of intelligence, sensory perception and motor control but it was also regarded as the source of pleasure and pain, the origin of emotions, and the font of moral judgment and aesthetic experiences.

Secondly, Plato's tripartite conception of human soul. According to this notion, each part of the soul localized to different body sites and was linked to distinct anatomical structures.

Although partly derivative and not central in the Greek biological and medical tradition, this hierarchical, highly ideological subdivision, with the brain in a pre-eminent position, was an organic attempt to distinguish different psychic faculties and to link them to specific structures. We can establish a tentative relationship between the diverse soul species identified by Plato and the functional properties of distinct neural compartments as clarified by modern investigation. In this context, the rational soul would correspond to neocortical functions whilst the emotional soul would be more related to limbic activity. The vegetative soul would partly correspond to the hypothalamus and the peripheral autonomic nervous system.

The third most admirable contribution is to be found in Herophilus' and Erasistratus' discoveries. The modern approach to the dissection of the nervous system, the clear description of many neuroanatomical structures, the identification of cranial and spinal nerves and the fundamental distinction between sensory and motor nerves represented the legacy of these great researchers to the development of neuroscience.

Worth of particular mention was Erasistratus' hypothesis of a possible relationship between the intelligence of man and the number and complexity of the convolutions of his brain. Regrettably, this remarkable observation was scornfully discarded by Galen, who claimed that even the ass' brain presented numerous convolutions. In Galen's pneumatic physiology it was the psychic pneuma to be endowed with the properties now attributed to neurons [37,38]. Had Erasistratus' conjecture been further and properly investigated, the history of neuroscience could have run a different way.

The weight of Greek heritage was enormous. The controversy between encephalocentrists and cardiocentrists continued well into Renaissance and beyond. It often took the form of a contention between Galenism and Aristotelism. Still in 1628, Harvey (1578–1657) wrote in *De motu cordis et sanguinis in animalibus* that the heart was the centre and the sun of the body microcosm and the source of sensitive, motor and vegetative life [25]. He was in polemic with the encephalocentric view of his master Hieronymus Fabricius of Acquapendente (1533–1619) who, in *De musculi actione*, claimed that the brain was the primary motor because it caused movement but it was unmoved.

In 1553, 75 years before Harvey's statement, the Spanish mystical physiologist Miguel Servetus (1511–1553) had reasserted the primacy of the heart and claimed that the blood was the seat of human soul. Aristotelian cardiocentric theories were harshly fought by the Galenist physician Jean Fernel (1497–1558) who defined them an unbelievable delirium ("*deliratio incredibilis*") [12]. These conflictual points of view testify how the dispute between encephalocentrism and cardiocentrism was still alive at the beginning of the modern scientific era.

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