Summary

From the Era of Pre-Socratic philosophers, soul and mind have been the subject of continuous speculation, study, research and meditation. Empedocles may be considered as the most approximate to Neurosciences Pre-Socratic philosopher. He was born in the city of Acragas (Agrigento) in Sicily in 492 BC, in the Era of the great Sicilian tyrants Hieron of Syracuse and Theron of Acragas. Empedocles was philosopher, physician and priest, mystic and prophet, poet of a high talent, brilliant orator, who attempted to associate religion, science, and politics for the social common good, a man characterized by generosity and magnanimity. He was adored by his compatriots, colleagues and the citizens of Acragas, as an exceptional person, very important, glorious, being beyond human mortality and temporality. Empedocles writings are mainly summarized in two poems, written in hexameter verse. One of them was entitled "On Nature" and the other "Purifications". During his life Empedocles searched for the pure and genuine knowledge and tried to find the answers of main questions and problems, which concern cosmogony, cosmology, ontology, anthropology, morality and ethics, human behavior and sociology. According to Empedocles there is not birth and death. There is only a connection or mixture and separation of four pure fundamental elements or "roots", which are the earth, the air, the fire and the water. Every time that the "roots" are connected together and interacted, life is created. Their separation is equivalent to decay, disintegration and eventually to death. The main forces of universal value which provoke the mixture and the separations of the four fundamental elements are Love and Strife. These are the eternal powers which control mixing and unmixing of all elements. The two powers exist and would exist for ever in a continuous opposition, exchanging and replacing each other in a round way, exercising a strong influence on the balance of the universe and the homeostasis of the human soul. The happiness and the exhilaration are attributed to Love, which is the omnipotent unifying force acting in balance and harmony. All the creation is based on the Love. Any endeavor for development of a harmonious, rational society, characterized by friendship, kindness and perfect collaboration is based on the Love. Empedocles claims that there was a stage in which Love dominated and all things were unified and intermingled into a Sphere, in a cosmic harmony. Unfortunately, Strife has separated the elements in a later time, inducing mortality and decay. That was the beginning of cosmogony. Everything suffers from the contradiction between Love and Strife, which are the active forces which control the cosmic cycle of continuous alterations. Without Love the man is a prisoner, enclosed in an unfamiliar tunic of flesh, an exile from the territory of harmony and serenity. Empedocles described the Globe (Sphere or Sphaera) as a god-like entity, as a prototype stereoscopic image of the unity and harmony, of the completeness and self-sufficiency, according to Orphic concept of friendly collaboration of all ingredients, which are connected together with the strong links of Love, composing the "One". Empedocles claims that ontogenesis under the power of Love results in creation of perfect entities, bodies and faces, whereas under the influence of Strife malformations and congenital defects are created in humans, animals and plants. Empedocles underlines that the continuous controversy between Love and Strife troubles and trials the human soul and disturbs the thoughts and the emotions. In the field of the biological sciences Empedocles' theory of the four "roots", which have an equal validity and importance, as the basic elements of creation, is of existential importance. In reality, based on the biological sciences, the harmonious coexistence of all Empedocles' "roots" is expressed nicely in the mitochondria of the cell, which are the most essential organelles for the living

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entities, the source of energy production and the main factor of cellular homeostasis, differentiation and continuity of life. Empedocles’ philosophy inserts in the depths of brain function, concerning emotion and behavior. It inserts in the limbic system, which is consisted of evolutionarily archaic brain structures closely associated with personality, morality, motivations, memory, emotions and human social behavior. Amygdala as anatomical structure is global like the “Spheros”, which was described by Empedocles. Neuronal circuits of amygdala are particularly involved in emerging emotion and behavior with the coordinated activity of many cortical and subcortical structure of the brain, including the prefrontal area of the frontal cortex, areas of the temporal isocortex and the hippocampus. A vertex enters and occupies the human soul whenever the Strife dominates in the world. Then the interior harmony and the homeostatic equilibrium are lost. The motionless tranquility and serenity of the Being are extinguished. They are replaced, as a rule, by fear, which is emerged from the amygdala under the influence of noxious exterior stimuli, which change the interior order and induce the anxiety, the instability, the fear, the threat and the existential insecurity. As long as the conflict between Love and Strife would last, the human being shall remain prisoner and captive of his own passions, unable to find the real root of his life, unable to establish the interior peace and harmony. In the field of the Neurosciences the fundamental feelings of Love and Strife are the two crucial poles of the extensive spectrum of the human emotions, playing an essential and decisive role in interior life and the behavior of the human being.

Keywords: Empedocles, Neurosciences, Neurophilosophy, Mitochondria, Limbic system, Amygdala

Introduction

Neurosciences are extended into a broad field, where the scientific observation and research join harmoniously the imagination, the intuition, the philosophy, the critic analysis, the enthusiasm and the skepticism. The foundations of the neurosciences from the very beginning were based on questions that the human being posed to himself, concerning the existence, the soul, the psychosomatic entity, the conscience and the knowledge of the world, the perception of time and space and mainly on problems which exercised the initial existential anxieties. Then the philosophy, which is the most advanced fine expression of human mentality and the neurosciences were tightly jointed together in a functional unity, where neurosciences have become the essential background of philosophy, and philosophy helped in detaching neurosciences from the limited mechanistic neurophysiological background, opening new horizons in the theoretic perspectives and new motivations for research, on the bases of an advanced multi-dimensional intellectuality.

From the Era of Pre-Socratic philosophers soul and mind have been the subject of continuous speculation, study, research and meditation. The emotions and the interior feelings of the soul, which play a dominant role on the human behavior helping in a deeper approach of the Being have been the focus of insisting endeavors for right interpretation and detailed analysis. The relationship between body and soul and the importance of the mental activities on the psychosomatic homeostasis are subjects of inquiry from the Greek antiquity up to our Era.

From the unique persistent endeavor of Heraclitus to dedicate all his life in order to discover his genuine and proper self in the context of Word or Logos and the study by Parmenides on the inter-
relationship between Being and Becoming\textsuperscript{7}, the initial roots of the Philosophy of Neurosciences\textsuperscript{8} were already implanted.

Empedocles would be considered as the most proximate to Neurosciences pre-Socratic philosopher. He was younger that Heraclitus and older than Socrates, born in 492 BC in the city of Acragas (Agragentum or Agrigento) in Sicily, one of the most prosperous and beautiful cities of the “Grecia Magna”, which was unfortunately destroyed by the Carthaginians in 406 BC. Empedocles endeavored to enter in the depths of the human soul in order to discover the interior power which dominates on the emotions, the feelings and the social behavior of the human being. Among the other components he identified the main poles of the emotional interactions. Thus Love and Strife are the ends of an axis\textsuperscript{9} which regulates and controls all the spectrum of the human emotions.

The man, as a part of the world is under the influence of many forces. Among them the Love and the Strife control the interior stability of everything. Love, equal in length and breadth, contributes in the friendly communication with the universe and the humanity and is essential for the establishment of the interior peace. The Strife is associated with the contradictory character, such as the ability to resurrect men who passed away and to control the nature. According to the legend, Empedocles died by throwing himself into active volcano Etna in Sicily, trying to prove his immortality and his god-like nature\textsuperscript{10}. However, the general opinion was that he was an extremely intelligent person, “a man of exceptional knowledge\textsuperscript{15}, inventor of rhetoric art, excellent physician, who introduced new and decisive therapeutic methods, a genuine intellectual and philosopher, a citizen of democratic Sicily, in the era of the great Sicilian tyrants, Hieron of Syracuse and Theron of Acragas. He was the son of Meto\textsuperscript{10}, who played a very important role in overthrowing the tyranny and establishing the democracy in Acragas, in 470 BC. Empedocles was physician\textsuperscript{11} and priest, philosopher, mystic and prophet, poet of a high poetic talent\textsuperscript{12}, a brilliant orator\textsuperscript{13} who has endeavored to associate religion with science, and has been involved in politics for the social benefit.

We do not know any detail of Empedocles’ life. Diogenes Laërtius’ records on Empedocles’ life are intermixed with myths, stories and legends of contradictory character, such as the ability to resurrect men who passed away and to control the nature. According to the legend, Empedocles died by throwing himself into active volcano Etna in Sicily, trying to prove his immortality and his god-like nature\textsuperscript{14}. However, the general opinion was that he was an extremely intelligent person, “a man of exceptional knowledge\textsuperscript{15}, inventor of rhetoric art, excellent physician, who introduced new and decisive therapeutic methods, a genuine intellectual and philosopher, a citizen of democratic

The life and the work of Empedocles

Empedocles was born, in 490 BC, at the prosperous city of Acragas (Agrigentum or Agrigento) in

\textsuperscript{7} The “Being” by Parmenides is a dynamic one, equivalent to “Becoming”. Being is the real background of becoming. Being includes the wholeness and the infinitive. Being would be on the way to perfection and to absolute.


\textsuperscript{9} B17 (Diels-Kranz).

\textsuperscript{10} Diogenes Laërtius H, 51, Satyros in his Lives claimed that Empedocles was the son of Exaenetus (fr. 11 FHG III 162) (DL 8.53)\textsuperscript{7}.

\textsuperscript{11} «Satyros said that Empedocles was physician (FHG iii. 162 sq.) and excellent teacher of rhetoric”. Diogenes Laërtius.H, 57.\textsuperscript{7} Diogenes Laërtius.H, 57. Galen characterizes Empedocles as a physician of the Italian school, Pliny as an empirical scientist, Celsus as an excellent healer, and Iamblichus as a skilled practitioner. Hermippus says that Empedocles healed the difficult case of Pantheia, a woman of Acragas, whom the other physicians were unable to treat (DL 8.69).

\textsuperscript{12} Aristotle writes in “On Poets” that Empedocles as a poet belongs to Homer’s school. He is very powerful in diction, in metaphors and in the use of all poetic styles (DL 8.58) but overall Empedocles is a scientist (Aristotle Poet.1.4447b 17, DK 31 A22).

\textsuperscript{13} Aristotle, in his Sophist, says that Empedocles was the first person who invented rhetoric, and Zeno the first person who invented dialectics.

\textsuperscript{14} Hippobotus said that when Empedocles got up, he set out on his way to Etna; then, upon reaching it, plunged into its fiery craters and disappeared, endeavoring to confirm the report that he had become a god. Afterwards, the truth was known, since one of his sandals was thrown up in the flames (DL 8.69). Timaeus contradicted this legend asserting that Empedocles left for the Peloponnesus and never returned. He insisted that Empedocles died in some unknown manner and his tomb was not found (DL 8.71). However a tomb in Megara attributed to Empedocles is mentioned by Favorinus. Osborne claims that the legend of Etna underlines the “various Dionysiac cults and mystery traditions” Osborne, C. 1987. „Empedocles recycled.” CQ 37: 24-50.

\textsuperscript{15} DK B129.
principles, characterized by generosity and magnanimity. Empedocles’ death at the age of 69 years was glorious, according to Aristotle, he was deified by his compatriots, in spite of the arguments for his mortal human nature. Empedocles writings are mainly summarized in two poems, written in hexameter verse. One of them was entitled “On Nature” and the other “Purifications”. The poem on Nature has an obvious cosmologic character, introducing at the same time the main principles of evolitional ontology. The other poem entitle “Purifications” has a strong religious character. From the two poems only 450 lines, in fragments, have been survived through centuries, which are strong enough for relieving the philosophical principles, the clarity of the mind, the enthusiastic character of the philosopher and the influences by Heraclitus and Parmenides.

During his life Empedocles searched for the pure and genuine knowledge and tried to find the answers of main questions and problems, which concern cosmogony, cosmology, ontology, anthropology, morality and ethics, human behavior and sociology.

Empedocles philosophical principles

According to Empedocles there is not birth or coming into existence and death. There is only a connection or mixture and separation of four pure fundamental elements or “roots”, which are the earth, the air, the fire and the water, identified with the symbolic names of Zeus, Hera, Nestis, and Aidoneus. These four essential ingredients are simple, unalterable, eternal and well balanced. Every time that they are connected together and interacted, they create life. Their separation is equivalent to decay, disintegration and eventually to death. Thus everything is the result of the interaction of the four elements. Nothing is autonomous or spontaneous. Nothing has a pure individuality.

There is no transition from the existence in to nothingness, but only a ceaseless interchange of successive existences, controlled by the alternating domination of Love and Strife. Therefore, there is no tragic aspect of death, since there is no death in the proper meaning. There is no nothingness and there is no existential vacuum. The main forces of uni-

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17. Diogenes Laërtius. Η,65).
19. Aristotle and Diogenes Laërtius claimed that Empedocles wrote also a hymn to Apollo, a poem on Xerxes “The invasion of Xerxes”, which is unfinished, political works, tragedies (Diog. Laërt. 8.57) and a Medical Poem extended to six hundred verses (DL 8.77). Neanthes claimed that Empedocles wrote the tragedies in his youth. (DL 8.57–58) The poem on nature exercised a profound influence on Lucretius and Cicero, as well as on other doxographers, like Aristotle and Simplecius. During the renascence Empedocles’ poems were translated in Latin by Xylander and published in Paris in 1573 by Stephanus. One of the best editions is that by Hermann Diels in Berlin in 1901, included in the collection Poetarum Philosophorum Fragmenta. In 1992, Alain Marten proved that fragment of a papyrus discovered in Pentapolis of upper Egypt and stored for nearly a century in the library at Strasbourg belong to Empedocles’ poem on Nature. See also Martin A, Primavesi O. L’Empédocle de Strasbourg, Berlin and New York 1999. See also Furley D. Variations on Themes from Empedocles in Lucretius’ proem. BICS 17 1970; 55-64.
22. Fragm.8
23. Fragm. 6. The number four or the tetractys has a very special symbolism in Pythagorean philosophy. Empedocles admired and respected profoundly Pythagoras. He wrote “There was a man among them of rare wisdom, who possessed the greatest treasure of knowledge. (DL 8.54; cf. Empedocles’ fr. 129). Some of Empedocles’ concepts may be attributed to Anaximander and Pythagoras, while his methodology may be attributed to Anaxagoras (Alcidamas ap. DL 8.56).
24. “Hear, first of all the roots of all things, which are Zeus and bright-shining Hera and Aidoneus who generates life, and Nestis too who, with her tears, moistens the mortal stream” (Fragm. 6).
25. Empedocles adds the earth as supplementary element to the water of Thales, the air of Anaximenes, and the fire of Heraclitus. According to Aristotle these four elements, which have been traditional in Greek physical theory (Aristotle, Met. A4, 985a31–3), were mentioned first by Empedocles. The theory of the four fundamental elements or roots is not far from the scientific reality, since earth symbolizes the carbon (C), the basis of any organic substance, the water (H2O) and the air (O2) are also essential elements of the life and the fire created from the union of carbon with oxygen is the source of energy for any activity in life (circle of Krebs).
27. Fragm.13.
versal value which provoke the mixture and the separations of the four fundamental elements are Love and Strife. These are the eternal powers which control mixing and unmixing of all elements. Love is the connecting power. The elements are united, blended and harmoniously intermingled under the beneficial agency of Love, which pervades the universe and acts as the moving power of the human life. Love and Strife are the main forces, which as divine powers motivate, modulate and control the human behavior. Love is the unifying power attracting and blending the "roots" in a compact and functional set, whereas the Strife induces the enmity, the hostility, the separation and the chaos. The two powers exist and would exist for ever in a continuous opposition, exchanging and replacing each other in a round way, exercising a strong influence on the balance of the universe and the homeostasis of the human soul. Those two forces control the continuous interchange of life and death.

The happiness and the exhilaration are attributed to Love, which is the omnipotent unifying force acting in balance and harmony, which penetrates the members of the human body and penetrates deeply the soul as a genuine purifying power. The unity and solidarity of the human existence are virtually based on the unifying power of Love.

All the creation is based on the Love and any tendency for development of a harmonious, rational society, characterized by friendship, kindness and perfect collaboration is also based on the Love.

Whenever Love dominates everything is even, smooth and symmetrical, like the surface of a globe (sphere or sphaera), which has the maximal capacity of the volume. Empedocles claims that there was a stage in which Love was dominant and all things were unified and intermingled one another into a Sphere in a cosmic harmony. Unfortunately Strife has separated the elements in a later time inducing mortality and decay. That was the beginning of cosmogony.

Strife causes alteration, transformation and separation of the global unity into separated masses which are destined to disintegration. Strife can separate even the members of the body and the elements of the soul.

Everything suffers from the contradiction and rivalry between Love and Strife, which are the active forces controlling the cosmic cycle of continuous alterations. The suffering of the universe and the anxiety and agony of the human soul never cease due to perpetual exchange of preponderance between Love and Strife, unless the connecting power of Love succeeds to dominate eventually establishing the peace, the friendship, the unity and the concreteness.

Without Love the man is a prisoner, enclosed in an unfamiliar tunick of flesh and an exile from the territory of harmony and serenity. He is far from the wealth of divine understanding, a servant of passions, of fear, of instability, of threat, succumbed to homicide.

Empedocles described the Globe (Sphere or Sphaera) as a god-like entity, as a prototype stereoscopic image of unity and harmony, of completeness and self-sufficiency according to Orphic concept of friendly collaboration of all ingredients, which are connected together with the strong links of Love, composing the "One" according to Parmenides. The Globe is a symbol of unanimity, equality, equivalence.

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28. Fragm.17,3
29. Fragm.17,20
30. Fragm.17,22
31. Fragm.19.
32. Fragm.21,8
33. Fragm. B 27
34. Fragm. B 35
35. See Aristotle On the Heavens II 13, 295a29 and On Generation and Corruption II 7, 334a5
and harmonious homeostatic state. On the other hand Globus may symbolize the generation of the soul and the eschatological restoration of everything within the bounds of harmony, tranquility and reason.

Empedocles, as natural philosopher, described the movement of moon around earth, the eclipses of sun, the fire in the depths of the earth, the atmosphere around earth.

As biologist, Empedocles described the chimeric creatures, the teratogenesis, the hermaphroditism of the body, the hybrid forms. He proceeded to detailed descriptions of morphological alterations, of separation of members of the body, which remind works of modern biologists and anthropologists and the consequences of the recent interventions in the human genome.

Empedocles claims that ontogenesis under the power of Love results in creation of perfect entities and faces whereas under the influence of Strife would produce malformations and congenital defects in humans, animals and plants.

The tissues of the body, the viscera and the limbs are composed by essential elements which are intermixed and interrelated in equivalence. Empedocles attempted to understand the physiology of respiration and the blood circulation, the function of the heart and the blood supply of the brain. He described also the material nature of air and the relationship between air and water in the bright metaphor of the double-bell (clepsydra).

Empedocles gives the impression that he is cardio-centric, concerning cognition and thoughts. However, he had the impression that heart is of substantial importance in supplying the brain with blood and energy, whereas brain is the center of cognition and the mental activities.

Empedocles' personality

It is very important to try to understand Empedocles' impressive and enigmatic personality. He was the poet, the philosopher, the politician, the physician and heale, the enthusiastic person and at the same time the melancholic eloquent man, the hierophant with divine properties.

It is very important to try to understand what Empedocles believed on himself. Initially the impression given might advocate that he considered himself as being above all humans, a god or god like being, due to his extraordinary capacities, knowledge and wisdom. He was endorsed by many qualifications and he was adored by his compatriots, colleagues and the citizens of Acragas and Sicily, as an exceptional person, very important, glorious, being beyond human mortality and temporality. It is true, that according to his biographers Empedocles was always an outstanding physician, very skilled and beneficial to others, very precious for his patients. He was also priest, prophet, orator, a wise man who overpassed the standards of his Era. However dis-
covering the Strife in himself, he admitted that he was a human being, mortal, wondering in the world like an exile and fugitive, in a condition of depersonalization, a simple miserable member of the creation inside the natural world, like a fish outside the sea. He considered himself as a dishonest detainee captive in a cave, as a slave to his passions and his interior conflicts.

Empedocles realized how a man is miserable and unhappy, due to his changeability, interior instability, uneasiness, frustration, mental fragility, fluidity of his interior life, incertitude, occupied always by strife and pain.

However, the knowledge and the wisdom elevate the human being and restore his ancient spiritual beauty. The interior harmony, the high mentality, the peace and serenity of the soul shine and pacify the human society. Blessed is he who possess the treasure of wisdom and his thoughts are inspired by divinity.

Empedocles recognized in a state of self-evaluation, that in spite of the continuous efforts for spiritual culture and wisdom, it is very hard, even impossible, for the man to approach the divinity. Although defication might be the center of the meditation, perspectives and expectations of the human being, it is unfeasible practically, since God is Spirit, a Mind impossible to be described by man, beyond any anthropomorph and anthropometric character. It is enough for the human being to avoid malevolence and to adapt his human nature peacefully, endeavoring to culture the virtues and the spiritual values perpetually.

Empedocles as Neuroscientist

Empedocles underlined that the continuous controversy troubles and trials the human soul and disturbs thoughts and emotions.

It is true, that problematizing and disputing are essential in scientific research especially in the field of Neurosciences. Many years after Empedocles' philosophical contribution, the skeptics, such as Sextus Empiricus claimed that controversy is the theoretical basis of Science and Philosophy and he tried to deliberate the thinker from the dogmatism and the anxiety and depression, which are derived from the fixation on inflexible doctrines and axioms, encouraging him to proceed to continuous search for the truth.

In the field of the biological sciences Empedocles' theory of the four "roots", which have equal validity, as the basic elements of the creation of the life is of existential importance.

The earth, the fire, the air and the water are the essential elements of living creatures. They symbolize at the same time the unity and the multiplicity. The lack or the separation of one of them is incompatible with the continuation of the life.

64. Empedocles declares himself depressively "an exile from the gods and a wanderer" DK B115.13. In the journey of the life Empedocles is one of the men, who are "interchanging their paths" between immortality and mortality. DK B35.15.

65. Fragm.118.

66. In that concept, the influence of Orphic doctrines is obvious. It reminds also the Platonic parable of the cave (Plato Politeia Z.514a). There is an "esoteric network" according to Kingsley, which includes the Pythagorean tradition, the Sicilian mythology, the mysteries of Persephone, the Bacchic gold plates and the Orphic texts. See Kingsley P. Ancient Philosophy, Mystery and Magic. Oxford 1995, Edmonds RG. Myths of the Underworld Journey. Plato, Aristophanes, and the 'Orphic' Gold Tablets. Cambridge 2004.

67. Fragm.124.

68. Correl. «Every good gift and every perfect gift is from above, and cometh down from the Father of lights, with whom is no variableness, neither shadow of turning» James 1,17.

69. Fragm.121

70. Fragm.145

71. Correl. "and the peace of God, which passeth all understanding, shall keep your hearts and minds through Christ Jesus". Phil.4,7

72. Correl. "O the depth of the riches both of the wisdom and knowledge of God! how unsearchable are his judgments, and his ways past finding out!" Rom.11,33

73. Fragm.132

74. Fragm.133

75. Correl. "For who hath known the mind of the Lord? or who hath been his counselor?" Rom.11,34.

76. Empedocles, like Heraclitus and Xenophanes reject the anthropomorphic character of divinity. See also Xenophanes Fragm. 11-16 and 23.

77. «you should fast from malevolence » Fragm.144.

78. Correl. "According as his divine power hath given unto us all things that pertain unto life and godliness, through the knowledge of him that hath called us to glory and virtue" 2 Peter 1,3.

79. Purifications Fragm.114.


82. Fragm.B6

83. Fragm.B17,27

84. Fragm.8
The mitochondrion

The harmonious coexistence of all Empedocles’ “roots” occurs in the mitochondria of the cell, which are the most essential organelles for the living entities, since they are the source of energy production and the main factor of cellular homeostasis, cellular differentiation and of the continuation of the viability of the cell.

The Empedocles’ four roots are connected tightly in the membrane systems of mitochondria. The “earth” symbolizes the proteins, the lipids, the calcium, the iron and the other metals and ions of the outer and inner mitochondrial membranes and matrix. The main role of mitochondrion is the production of ATP from glucose. The energy production by glucose metabolism, as well as the electron transport chain represent Empedocles’ “fire”, which never ceases as long as the cell is alive. The “air” which symbolize the oxygen (O2) is essential for oxidative phosphorylation and redox reactions through electron transport chains in the inter-membrane system of mitochondria. The “water” is continuously produced in the mitochondrion by cytochrome c oxidase, (complex IV), which is the final protein complex in the respiratory chain and transfers electrons to oxygen, establishing therefore an electrochemical equilibrium in the cell.

The role of Calcium homeostasis by mitochondrial activity is essential for the viability of the cell and the cell signaling, which is of fundamental importance for the neurons, which continuously exchange informations, in the context of numerous short or long neuronal circuits, using large number of neurotransmitters, receptors and ion channels. Mitochondrial activity protests the cell from excitotoxic degeneration and eventual apoptosis, which would have tragic consequences for the function of the brain. On the other hand calcium, “the earth”, in mitochondria contributes in energy production, “the fire”, activating the enzymes of the oxidative phosphorylation to reform ATP.


86. The “proton leak” in the mitochondrion, which is mediated by a proton channel called thermogenin contributes also in heat production. See also Mozó J, Emre Y, Bouillaud F, Ricquier D, Crisculufo F. Thermoregulation: What Role for UCPs in Mammals and Birds?”. Bioscience Reports. 2005; 25 (3–4): 227–249.

87. The Empedocles’ four roots are connected tightly in the membrane systems of mitochondria. The “earth” symbolizes the proteins, the lipids, the calcium, the iron and the other metals and ions of the outer and inner mitochondrial membranes and matrix. The main role of mitochondrion is the production of ATP from glucose. The energy production by glucose metabolism, as well as the electron transport chain represent Empedocles’ “fire”, which never ceases as long as the cell is alive. The “air” which symbolize the oxygen (O2) is essential for oxidative phosphorylation and redox reactions through electron transport chains in the inter-membrane system of mitochondria. The “water” is continuously produced in the mitochondrion by cytochrome c oxidase, (complex IV), which is the final protein complex in the respiratory chain and transfers electrons to oxygen, establishing therefore an electrochemical equilibrium in the cell.

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ed with aging and a substantial number of neurological debilitating disorders, such as Alzheimer’s disease\textsuperscript{100,101}, Parkinson’s disease, Huntington’s chorea\textsuperscript{102} and many others, which provoke tragic deterioration of the quality of life.

The limbic system. The amygdala

Empedocles’ philosophy inserts in the depths of brain function, concerning emotion and behavior. It enters in the limbic system\textsuperscript{103}, which is consisted of evolutionarily archaic brain structures, closely associated with personality, morality, motivations, memory, emotions and human social behavior\textsuperscript{104}.

The two poles of the human emotional activity and moral consciousness, which play the most important role in the interior life and social behavior, are the feelings of Love and Strife, so extensively emphasized by Empedocles. Both of those feelings are related to neuronal circuits of limbic system and the other emotion-memory related neuronal structures of the brain\textsuperscript{105}. Neuronal circuits of amygdala are particularly involved\textsuperscript{106} in emerging emotion and behavior with the coordinated activity of many cortical and subcortical structures of the brain\textsuperscript{107}, including the prefrontal area of the frontal cortex\textsuperscript{108}, areas of the temporal isocortex\textsuperscript{109} and the hippocampus\textsuperscript{110}.

In the anatomical areas of amygdala, the basic lateral nucleus (BLA) seems to play an important role in the differentiation of the primitive emotional impulses, on the basis of the senso-sensorial experiences of the individual\textsuperscript{111}, whereas the central nucleus is mostly involved in emotional reliability and responses of the autonomic nervous system to emotional impulses. Therefore Love and Strife are reinforced by exterior stimuli, related to environmental conditions. The orbitofrontal cortex is also important in the modulation of behavior, under emotional impulses, associated with external visuo-auditory and olfactory stimuli. The posterior cingulate cortex plays a crucial role in supporting internally-directed cognition and in modulating social behavior, in collaboration with anterior cingulate cortex, which is involved in emotional regulations and self-transcendence\textsuperscript{112}, exteriorizing either Love or Strife.

Amygdala, as an anatomical structure, is global like the “Spheros” described by Empedocles\textsuperscript{113}. Under the feeling of Love and the positive emotions the human being is solid and compact, since the connective power of the love, associated with happiness makes tight links among the elements of the entity, resulting in a harmonious unity of the soul, like globalism of the being.

Later on during the life, whenever negative emotions, like Strife, penetrate the soul, an alteration of the simplicity and unity of the soul occurs, resulting in...


\textsuperscript{101} See also Baloyannis S. Alterations of Mitochondria and Golgi Apparatus Are Related to Synaptic Pathology in Alzheimer’s Disease. In: Uday Kishore (Ed) Neurodegenerative Diseases In Tech, ISBN 978-953-51-1088-0. DOI: 10.5772/45957.


\textsuperscript{104} See also Baloyannis S J: Human consciousness from the neurobiological view point. In: Nicolaides A (Ed) The worlds of Science and Religion. Thessaloniki 2008, pp.91-116.


\textsuperscript{106} The knowledge of the important role of the amygdala in emotion, memory and behavior is based on the work of Klöver and Bucy in 1937, the seminal works of Papez, Weiskrantz, Yakovlev and MacLean, Hilton and Zbrozyna, 1963. That concept has endured to the present day. See also Mesulam MM. Behavioral neuroanatomy: large-scale networks, association cortex, frontal syndromes, the limbic system, and hemispheric specializations. In M M. Mesulam (Ed.), Principles of behavioral and cognitive neurology (2nd ed.) Oxford: Oxford University Press 2000. pp.1-120.


\textsuperscript{111} The experienced rewards and punishers are very important reinforcements of the emotions. See also Rolls E T. Emotion and decision-making explained. Oxford: Oxford University Press, 2014.


\textsuperscript{113} Fragm.B28-29. The “Sphere” of Empedocles is a parallel concept with the “Globe” of Parmenides. Both of them symbolize the absolute harmony, the interior connection, the compactness, the plentitude and the capacity of further augmentation and extension, without any alteration of the shape. Both of them express the unity and the solitude of “Being”
an obvious fragmentation of the being. The negative emotions are emerged from the structures of the limbic system. The augmentation of the Strife results in the augmentation of the interior contradictions and the fragmentation of the global solidity of the soul\textsuperscript{114}. A vortex occupies the soul\textsuperscript{115} whenever the Strife dominates in the world and in the human soul. Then the interior harmony and the homeostatic equilibrium are lost. The motionless tranquility and serenity of the Being is lost. It is replaced, as a rule, by fear, which is emerged from the amygdala\textsuperscript{116} under the influence of noxious external stimuli\textsuperscript{117} which change the interior order and induce the anxiety, the instability, the fear, the treat and the existential insecurity.

The dramatic phenomena of the conflict of emotions in the human soul, the interior contradictions, the multiple and multiform alterations, the fluctuations of the mood and behavior are the tragic consequences of the rivalry and perpetual antagonism between Love and Strife. The Love unifies\textsuperscript{118}, composes, harmonizes, combats the fear and the tread\textsuperscript{119}, constructs\textsuperscript{120}, globalizes, establishes the truth in the consciousness of the human being\textsuperscript{121}, induces the liberty, the friendship and the fraternity in the human society, directs the man’s efforts to peace, kindness, solidarity and compassion\textsuperscript{122}, whereas the Strife induces the interior fragmentation, the deceit, the envy\textsuperscript{123} the unsteadiness and the ceaseless fluctuations, the changeability of mind\textsuperscript{124}, the anxiety, the hostility, the anger, the social aggression and the interior decay, eventually\textsuperscript{125}.

As long as the conflict between Love and Strife would last, the human being shall remain prisoner and captive of his own passions, unable to find the real root of his life\textsuperscript{126}, unable to establish the interior peace and harmony.

In conclusion

Empedocles is a prototype of moral philosopher as well as a neuro-philosopher\textsuperscript{127}. He attempted to interpret the reason of the continuous alteration of the human emotions and the perpetuous conflict between Love and Strife, in the depths of the human existence. He claimed that the dispute and rivalry between Love and Strife is the main cause of interchange of happiness and pain, peace and aggression, kindness and envy, friendship and enmity, serenity and anxiety, unity and fragmentation, hope and despair, integrity and decay in the human life. Empedocles attempted to enter in the depths of the human soul\textsuperscript{128} in order to know and understand the most interior mystic feelings and to explain some of the phenomena of the human behavior. His philosophical doctrines associate harmoniously many concepts of Heraclitus and Parmenides projecting them in a new philosophical and poetical profile.

Empedocles endeavored to approach the truth. He used the myth, in a symbolic way, in order to emphasize the truth, offering it in a comprehensible, vivid and schematic way.

Empedocles exercised an important influence in the European philosophy. Thinkers like Kant and Nietzsche\textsuperscript{129} irradiated widely Empedocles’ philosophical doctrines. In Nietzsche’s philosophy good and evil, the strength and the weakness, the freedom

\textsuperscript{114} Fragm. B30
\textsuperscript{115} The vortex according to Empedocles is a whirling mass, which occupies the human soul as it occupies the nature like a cloud in a continuous motion, which disturbs the motionless harmony of the interior peace.
\textsuperscript{116} The fear as negative emotion is emerged mostly from the left amygdala (Funayama, Grillon, Davis, Phelps, 2001) either ingeniously or by exterior stimuli. The conscious recognition, that the fear is a suppressive noxious factor for the psychic activity, needs the collaboration of the amygdala with the hippocampus (Bechara et al., 1995).
\textsuperscript{117} See also Öhman A., Mineka S. Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. Psychol Rev. 2001;108 483–522.
\textsuperscript{118} For the love of Christ constraineth us; because we thus judge, that if one died for all, then were all dead 2 Cor. 5,14.
\textsuperscript{119} “There is no fear in love; but perfect love casteth out fear: because fear hath torment. He that feareth is not made perfect in love”.1 John 4,18.
\textsuperscript{120} “Knowledge puffeth up, but charity edifieth”. 1 Cor.8,1 121. “... in truth and love”.2 John 3.
\textsuperscript{121} “that with well doing ye may put to silence the ignorance of foolish men” 1Peter 2,15.
\textsuperscript{122} “Being filled with all unrighteousness, fornication, wickedness, covetousness, maliciousness; full of envy, murder, debate,..
and the subordination of the Apollonian and the Dionysian spirit interchange and dispute like the Empedoclean Love and Strife, modulating human behavior.

In the field of the Neurosciences the fundamental feelings of Love and Strife are the two poles of crucial importance in the extensive spectrum of the human emotions, which play an essential and decisive role in the character of interior life and the quality of his social behavior. Love and Strife are localized and emerged in the structures of the limbic system, one of the most archaic neuronal circuits of the brain, in the global nucleus of amygdala and the global structures of mammillary bodies.

Although Alcmaeon from Croton is considered as the first neuroscientist and neuro-philosopher, in reality Empedocles is the philosopher who entered in the depths of the human soul, attempting to interpret the motives of the patterns of the human behavior. Empedocles is the first neuroscientist who, in a symbolic and vivid schematic way, described the “sphere”, the global and circular shape of the limbic system, as being the center of the feelings and the human behavior, and a place of contradictions and interior conflicts between love and hate, peace and fight, calmness and fear, tranquility and uneasiness, good and evil, symmetry and asymmetry.

Empedocles describing all the fluctuations of the feelings, and the ceaseless search of the soul for peace, love, serenity, unity and homeostatic equilibrium, described actually indirectly the function of amygdala nucleus, sharply dissecting the limbic system with the acuity of his mind. He described schematically the shape of the center of the emotional harmony as a “spere” a globe, which also symbolizes the solid unity of the human existence under the domination of Love. Empedocles describing the vortex underlined the continuous fluctuations of the mental activities and introduced the concept of neuronal plasticity, which plays a substantial role in the behavioral adaptation and the interior culture of man.

132. Wachtler J. De Alcmaeone Crotoniate, Leipzig: Teubner 1896. Alcmaeon was the first who noticed that brain is the center of cognition. He made a precise distinction between sensation, perception and understanding. He believed that the senso-sensory organs communicate with the brain and transmit afferently the sensory impulses via the cranial nerves. Following the perception, the brain memorizes the sensorial stimuli, which become a part of his senso-sensorial experiences. The balance of the powers is the essential background of the health, whereas the domination of one power the “monarchy” is the main causative factor of the disease. See also Ebner P. Alcmeone Crotoniate , Klearchos, 1969;11: 25-77.

133. The limbic system or Broca’s limbic lobe includes the amygdala, the hippocampus, the septum pellucidum, part of the hypothalamus, the anterior nuclei of the thalamus, a part of the basal ganglia and the epithalamus. It is composed mostly of ring like connective structure, the so called Papez’s circles and numerous nuclei. Among them the global amygdala is a principal center, which plays instrumental role in the emotional procedures and the emersion of behavior. See also MacLean PD. The limbic system ("Visceral Brain") and emotional behavior AMA Arch NeuPsych. 1955;73(2):130-134.
134. FrAgm.8.
136. FrAgm. 27.
138.FrAgm. 17.
139. FrAgm.106. See also and Churchland P. Scientific Realism and the Plasticity of Mind. Cambridge: Cambridge University Press 1979.
140. FrAgm.35,10
31. Duchen MR. Ca(2+)-dependent changes in the mitochondrial Ca(2+) uptake in apoptosis. Cell Calcium 2006; 40: 31-34.
35. Furley DJ. Empedocles and the clepsydra. JHS 1957; 77: 31-34.
44. Hirz J. Energy transduction by respiratory complex I, an


47. Karsten S. Empedoclis Agrigentini carminum reliquiae, Amsterdam, 1838.


