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EDITORIAL
History of neuroscience in Greece: from Alkmaion to austerity

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In the frame of an historical section of the 2015 Featured Regional meeting of FENS in Thessaloniki, I was asked to talk on the 'History of Neuroscience in Greece'. Realizing the impossibility of the task, I focused on only two points: the dawn of neuroscience in Greece and the current situation which threatens the survival of neuroscience in Greece. Both points are closer to provocative questions than to evidence-based conclusions.

The dawn of neuroscience in Greece

What was the one most important contribution ancient Greeks offered to neuroscience? I think this contribution was nothing more and nothing less than daring to look for the (observable) bodily, as opposed to any (believed as) divine, causes behind human behavior and its disorders; a bold idea for that time, judging by the centuries it took to gain acceptance by the layman. Let us see it by the example of epilepsy: As early as 7th and 6th centuries BC, seizures were astutely diagnosed and described by Babylonians and Chinese according to their different clinical types; each attributed to, or protected by, a specific deity. Greeks of the pre-Socratic era did two contradictory things: superficially they adopted these religious beliefs of the East in coining the term 'epilepsy' (from 'επιλαμβάνειν', meaning the state of being possessed, seized), but at the same time, they undermined these myths by searching for the bodily mechanisms underlying the symptoms of a disease, which they were convinced not to be sacred, but due to a defective brain. This conviction allowed Hippocrates to make the next step after the vivisection studies practiced at his time. He conceived the idea of research in animal models of disease (specifically, he proposed examining the brain fluids of the epileptic goat). However historical this conception of a fundamental approach of modern neuroscience may have been, it did not materialize. The first experiments with animals had to wait for six more centuries (when Galen demonstrated loss of vocalization in piglets after lesion of the recurrent laryngeal nerve). For the first time it was demonstrated in a reproducible experiment that a specific behavior is controlled by the brain, unequivocally ascribing function to known structure.

Obviously, this change in attitude was the fundamental prerequisite for starting any experimentation on the brain. But when and where was it first conceived and by whom? It all started in Croton in Magna Grecia (in southern Italy of today, Fig. 1) where Alkmaion (~450 BC), a Pythagorean, was the first to dissect and study the anatomy of the brain and peripheral nerves. Based on his observations, he believed that the brain was the site of sensation and cognition, i.e. he grasped the idea that the optic nerves were 'light-bearing paths' to the brain. According to Robert Doty (2007), 'Alkmaion's idea that the brain creates the mind is a revolution in human knowledge comparable to that of Copernicus and of Darwin'. Alkmaion's encephalocentric views were adopted by Pythagorians, Philolaos and Hippon. Shortly after in Avdera in Thrace, the philosopher-scientist, Democritos (~425 BC), believed that the psyche is made up of the lightest, most spherical, and fastest-moving of his atoms, which are especially numerous in the brain. He dissected the brain of cats and he made very accurate drawings of the retina. In Klazomenae, Anaxagoras ascertains that '[the] center of the senses is the brain which develops first *in utero*'. In Kos, Hippocrates demystifies epilepsy. Erasistratus from Chios and Herophilos in Alexandria (300–260 BC), distinguished nerves from arteries and veins, described the cerebral ventricles and other neuroanatomical features, and proposed that 'pneuma' passed along the nerves. The encephalocentric views were corrected and further expanded by the great Greek physicians, Galen of Pergamon and Aretaeos of Cappadocia in Rome in the 2nd century AD. The consideration of the brain as the instrument of perception, memory, emotions and all mental activities as proposed by Alkmaion and Hippocratic physicians and their successors was made at that time and, of course, is the current main dogma of neuroscience.

The question arises: why were all these astute observations and concepts about the brain developed in the periphery and not in the center of the then known world? In Athens' Schools of philosophy, Socrates advocated a rational rather than empirical approach to the truth and he was a dualist, i.e. he thought that the mind is composed of a different substance to the brain. Plato, like Alkmaion and the Hippocratic physicians, supported the concept of the primacy of the brain in mental activities, placing therein the immortal part of the soul. However, he did not trust the senses and believed the truth derived from innate ideas. Plato's Academy thus had relatively little interest in the brain and its mechanisms. What mainly embarrassed, disappointed and puzzled many historians and scientists (including Sherrington) was that Aristotle, the founder of experimental science and father of psychology, for all his biological research, abandoned the brain for the heart as the seat of sensation. Plato's pupil, Aristotle and his famous Lyceum, rejected Plato's and Alkmaion's ideas and ascribed to the brain the supporting role of cooling the blood. The great philosopher's most startling error went against the founding principle of neuroscience, then and now. Ignorance of encephalocentric arguments can be excluded as a cause as he debates them in his works. A likely explanation (Gross, 1995) is that Aristotle lacked an essential approach to brain: he did not study the brain-injured human. The evidence that both Alkmaion and Hippocrates gave in favor of their encephalocentric view were strictly clinical, the prime source of information at the time as experiments on the brain did not start until Galen. Aristotle, although the son of

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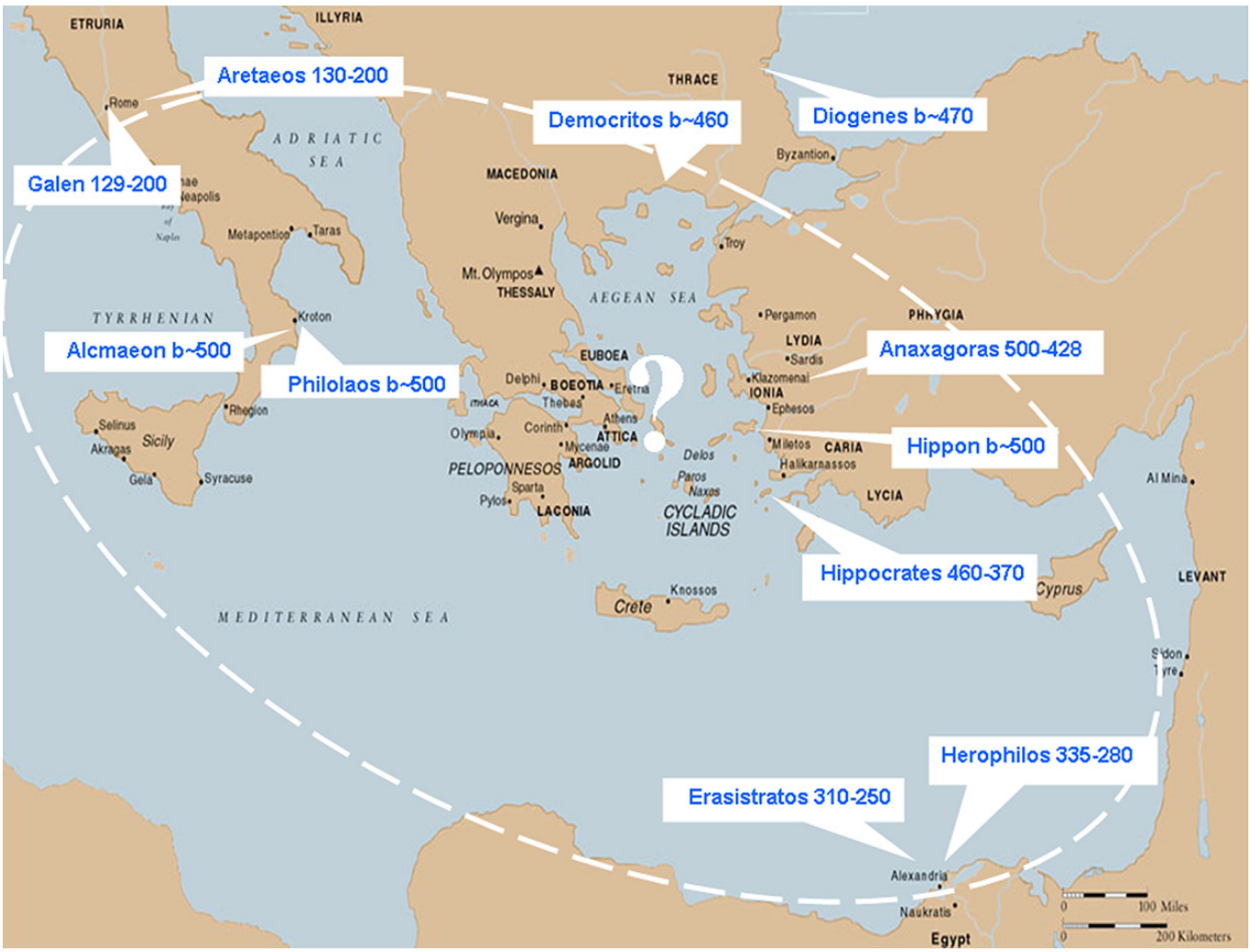

FIG. 1. Map of the eastern Mediterranean with the cities of the ancient era of 5th century BC to 2nd century AD. The names of philosophers who advanced the encephalocentric view are depicted along with a pointer to the place of their teaching. b~ stands for born circa. It is astonishing that these advances, which founded neuroscience, were made entirely in the periphery of the ancient Greek world, while at the center, the giants of philosophy were either little interested (Plato) or negative (Aristotle's cardiocentric view). Why?

an eminent physician, rejected medical training and never dissected a human. However, one has to admit that this 'error' had such deep roots in popular beliefs, that it survived tenaciously strong for many centuries and across several cultures (the debate between encephalocentric and cardiocentric theories continued from the ancients through the Arab scholars to medieval and renaissance Europe, e.g. Avicenna in the 11th century AD proposed a combination of the encephalocentric and cardiocentric views (Gruner, 1930), and Portia in Shakespeare's Merchant of Venice (1600) sings 'Tell me where is fancy bred, or in the heart or in the head'. One can therefore imagine additional factors contributing to Aristotle's misconception, like the prevailing philosophical attitude toward dying, which created reverence (and dread) of the dead human body and thus prohibited the study of cadavers. Besides that, the Athenian democracy had recently executed Socrates for his teaching and Aristotle may have had reason to feel insecure as a non-Athenian (he was born in Stagira/Chalkidiki) and was therefore less prone to adopt groundbreaking and probably unpopular ideas.

The puzzle of Aristotle's error may never be solved, but it seems that two lessons can be learned even from that early time of neuroscience. First, neuroscience has to integrate evidence from all disciplines including clinical observations or it may err fundamentally. Secondly, the development of novel paradigms in neuroscience is a difficult and vulnerable process, subject to prevailing bioethics and public beliefs with the power of established authority influencing even the greatest of minds.

Neuroscience in modern Greece

The 'Hellenic Society for Neuroscience' (HSN) was created in 1985 with the goal to help advance the neurosciences in Greece, i.e. advance relevant research and academic education as well as raising public awareness of the progress in brain research. Since 1990, HSN has been a member of International Brain Research Organization and since 1998, a founding-member of FENS. HSN currently consists of 447 members, 56% of which are women, who come from all kinds of disciplines and share an interest in understanding the brain, healing its disorders or creating brain-like machines. Greek Universities currently run 11 graduate studies programs which are either dedicated exclusively to neuroscience or contain an elective component/orientation on neuroscience. In the past 20 years, more than 250 PhDs have been awarded in the field, with about

60% in molecular, cellular and developmental neuroscience and about 15% in systems neuroscience. In the past decade, a large number of young scientists were trained in HSN members' laboratories: 258 undergraduates, 195 M.Sc. candidates, 212 Ph.D. candidates and 123 postdoctoral fellows. The official website, www.hsfn.gr, is a great help in that it hosts important educational documents, members' directory, announcements of meetings, scholarships, awards, research resources, graduate studies programs, forums, e.g. for debating on the proper translation of new neuroscience terms into Greek, public awareness activities in collaboration with the DANA alliance, and many more.

The neuroscience research output of laboratories and clinics in Greece is relatively meager ranking 17th in Europe, [A Scopus search in the last 50 years found 8652 papers bearing the entry 'Neuroscience' with country affiliation 'Greece' as compared to 1.899.807 with undetermined affiliation (0.45%). In the last decade 2005–2015 $n = 7111$ of 1 252 773 (0.58%). Scopus returned 15 208 papers with subject 'Neuroscience' and author names typically Greek (*opoulos, *akis, *idis and *ides). Of these, 43.83% had an affiliation in USA and only 25.56% had the country affiliation, Greece. A duration of 24 years back, this was 10% (Kostopoulos, 1992)]. However, there is some optimism for the future based on that the fact that most of these papers were published in the last decade and under conditions of relatively scarce financial support. In particular, the years 2000–2007, show a steady and rather steep increase in neuroscience publications from Greece (Fig. 2). A deceleration appears in the subsequent years affecting all science publications but especially neuroscience papers. Citations also seem to have plateaued but with a delay. The phenomenon is observed for all Greek publications, not just neuroscience, and is not evident for other countries like USA or Israel. Should one consider this deceleration of published research as a sign (an omen sent not from Zeus - but from Scopus) foretelling a decline of neuroscience in Greece? Alternatively could this be a normalization following an exceptionally good decade? The answer may come indirectly from studying recent developments in fields relevant to research.

In the wake of nation's debt crisis in 2010, fiscal austerity measures were imposed and they continue in spite of being admitted as ineffective and even counter-productive or even refueling the recession. Certainly, research and education have been increasingly neglected in the last few years (Abbott, 2015; Kollias & Lambris, 2015). There were drastic cuts in posts for teaching, research, technical and supporting personnel – there have been almost no replacements of vacated posts in the last 10 years. Support of universities and research institutes went down to 50%, while total research funding decreased even further from the disappointing 0.6% of Greece's gross domestic product (NDC, 2015). Needless to say, the consequence is the outdating and deterioration of research equipment, the suspension of libraries' subscriptions to major scientific journals etc. Austerity – or its invocation – led to an increase in bureaucracy in research administration, to myopic obsession with applied research and to continuing inability to create an independent state agency regularly providing support for basic research as the necessary foundation of applied research. Finally, an existing problem, 'brain-drain', accelerated. An estimated 150 000 scientists and professionals have already left the country and the trend increases – especially 'doctors leave Greece in droves' (Abbott, 2015).

An important and relevant consequence of the crisis/austerity is the toll on public health: between 2008 and 2015, the federal spending on hospitals fell from 6.3 to 3.9% of the GDP. Although Greece is not yet 'on The Verge of a Health Catastrophe' (Brozak, 2015), '5 years of austerity has taken its toll on Greek health care' (Karamanoli, 2015). The mean overall suicide rate rose by 35% in just 2 years (2010–2012) among persons of working age, a change that correlates with the rise in unemployment and coinciding with austerity measures (Rachiotis *et al.*, 2015).

The causes and consequences of the imposition of austerity measures are very complex, certainly political, going beyond any country's borders and certainly beyond the scope of this article. Several scientists have recently expressed, besides their agony, recommendations for an escape from the vicious cycle of recession and austerity (Editorial, 2013; Karamanoli, 2015; Kollias & Lambris, 2015; Rachiotis *et al.*,

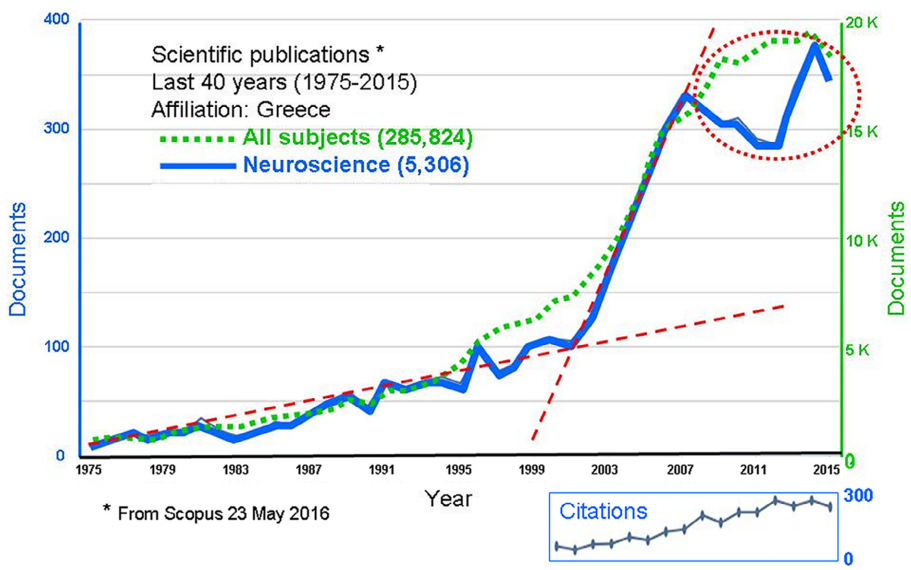

FIG. 2. Number of publications from Greece in the last 40 years. Note the different scale for total papers (green dotted line) and for papers with the subject 'Neuroscience' (blue line), according to Scopus categorization. Both show an acceleration around 2000 and a deceleration after 2007–2008 (red circle). No deceleration was observed in similar curves for neuroscience papers from Israel or published by authors of the Greek diaspora (Scopus data not shown). The number of citations of neuroscience papers from Greece between 2000 and 2015 seems to plateau after 2013.

2015). The Greek state ought to make evidence-based restructuring in universities and research institutions and grant them true autonomy, well-defined responsibilities, consequential evaluations and the substantial and regular support they deserve. They in turn should improve their record of devotion to excellence, restructure their curricula, research targets and collaborations, by investing in young minds and innovation opportunities. Certainly, facing poverty, unemployment and problems related to health, education and social justice are immediate priorities. Beyond that, science and development efforts should be excluded from the austerity measures, so that we can work on systematic inadequacies that pre-existed this crisis and should not survive it. The challenge is to reverse the situation toward a positive reinforcement between sectors like enabling and supporting excellence, education, research and economic development. Particular losses may be changed into advantages. For example, the numerous eminent neuroscientists in the Greek diaspora (see above) may help educating the brightest of our graduates. Also, niches of neuroscience should be explored, like development and applications of neuroinformatics, which are expected to spearhead economic development (OECD, 2002) and are suited to a country with the characteristics of Greece.

It is obvious that austerity constitutes an indirect and multifaceted threat to brain research; so serious that the productivity curve of Fig. 2 may be regarded as a sign of resilience of the Greek scientific community in the face of the described more general adverse conditions. It is hard to talk about austerity's adverse effects on brain research, while knowing that austerity threatens the brain itself (Noble *et al.*, 2015). However, research and development are the most promising allies to get us out of the crisis. Conducting high-quality research is neither inherited nor easily imported; it has to be continuously and locally fought for and achieved over and again. Any break in continuity will be detrimental and may be terminal; hence, the severity of the current problem. Urgently the threat to Greek neuroscience has to be faced. After all, an economic crisis is not a... 'sacred disease'. It has its causes and mechanisms, which we should understand and fight our way out.

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