

Constantin Tsiminakis (1875–1942): Neurologist, Neuropathologist, Statesman

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Running Title:

Constantin Tsiminakis (1875–1942)

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Abstract

The article is a 75-year memorial tribute to the Greek neurologist Constantin Tsiminakis (1875–1942). Coming from a family of physicians, Tsiminakis graduated from the University of Athens in 1897, and trained in Vienna under Nothnagel, Frankl-Hochwart, and Obersteiner. In 1905 he was appointed Reader in Neurology and Psychiatry at his alma mater. He published over 40 articles on neurological and neuropathological topics, including megalencephaly, hydrocephalus, progressive paralysis, epidemic encephalitis, dengue fever, and narcolepsy. However, his main focus of interest was epilepsy, including post-encephalitic forms. To differentially diagnose true from feigned epilepsy, he devised a method of compressing the carotids, which became known as the 'Tsiminakis maneuver'. A cultivated man and a talented poet, he rebutted the Freudian interpretation of artistic creativity. Finally, in the national legislative election in 1923, Tsiminakis was elected a Plenipotentiary Member of the Hellenic Parliament under the Liberal Party and served until 1925.

Key Words

History of neurology · Lothar von Frankl-Hochwart · Vienna school of neurology · Epilepsy · Tsiminakis maneuver · Neurology in Greece

Constantin Tsiminakis (Fig. 1, left) was born in Kozani (then in the Ottoman Empire, today in the region of Macedonia, Greece). His father, the physician Johannes Tsiminakis (1833–1907) was an alumnus of Vienna University and a statesman in Kozani. In 1887, the family took refuge in Athens when the Ottoman police discovered Johannes Tsiminakis' involvement in inciting and financing an insurrection; the family property was expropriated. Two other members of the Tsiminakis family also served as mayors of Kozani.

Constantin Tsiminakis graduated from the Second Gymnasium of Athens in September 1892. He enrolled in the Medical School of the University of Athens in February 1893, and obtained his doctorate in 1897. As a medical student, he volunteered as an intern in anatomy, and as an assistant in internal medicine. He specialized in neurology and psychiatry in Vienna and Paris (January 1898–July 1903), with short trips to London and Berlin [1, 2].

In Vienna, Tsiminakis worked as an assistant (*Aspirant*) under Hermann Nothnagel (1841–1905) in internal medicine, under Lothar von Frankl-Hochwart (1862–1914) in neurology, and under Heinrich Obersteiner (1847–1922) in neuropathology [1]. Returning to Athens, he taught at the University Neurology and Psychiatry Clinic of Aiginiteion Hospital, and headed the Neurology Department of the National Dispensary. He defended his *Dozentur* ('dissertation of habilitation') before the medical faculty of the University of Athens in December 1904, and was appointed, effective 1905, Reader in Neurology and Psychiatry. In 1907 he co-founded the private clinic *Galen* in Patissia in central Athens, together with Lecturer and fellow neurologist-psychiatrist Miltiades Oeconomakis (1875–1922); Tsiminakis headed this private clinic. The local university establishment subjected him to an investigation for simultaneously practicing medicine privately.

Tsiminakis befriended Constantin von Economo in Vienna and Georg N. Koskinas in Athens. When Economo died, a memorial session was held at the Athens Medical Society in November 1931, where Tsiminakis [3], and Koskinas, paid tribute to their eminent colleague.

In 1934, Tsiminakis was one of the six candidates (the other five were V. Konos, G. N. Koskinas, G. Pamboukis, J. Patrikios, and D. Triantafyllos) who petitioned for the vacant Chair of Neurology and Psychiatry, following the retirement of Michel Catsaras (1860–1939). The position was occupied by Georg Pamboukis (1885–1959), a fellow countryman from Corinth of Panagis Tsaldaris (1868–1936), the Prime Minister of Greece at the time [4].

Neurological Works

The times of Tsiminakis' life coincided with a tumultuous period in the life of Greece, exemplified by an entanglement in successive wars, including the Greco-Turkish War of 1897–1899, the Balkan Wars of 1912–1913, World War I, the Greco-Turkish War of 1919–1922, and World War II. Driven by the restlessness that has defined the Hellenic Diaspora throughout the course of history, many physicians sought an opportunity for specialty training abroad.

The University of Athens was founded in the newly independent Greek state in 1837. A landmark

in the evolution of academic neurology and psychiatry in Greece was the establishment in 1904 of the Aiginiteion Hospital in Athens, which housed, and continues to house to this day, the corresponding university clinics.

During his career, Tsiminakis published over 40 papers in German, French and Greek; several of these were in the *Wiener Klinische Wochenschrift* and about one-half of them in the *Proceedings of the Athens Medical Society*, of which he was elected councilor in 1926, and vice-president in 1931 [5].

Tsiminakis' first paper [6] concerned a case of megalencephaly in a child born with a remarkably large head and symptoms of rhachitis, but with normal development and intelligence, and without any obvious neurological signs. At 3 years of age, headache appeared, occasionally accompanied by vomiting. The head continued to grow in size uniformly, gradually reaching a circumference of 63 cm. Death occurred from scarlatina at the age of 8 years. At autopsy, after a day's fixation in 10% formalin, the brain weighed 1920 g; there was meningitis spread over the hemispheric convexity, extending from the forebrain to basal parts, ending caudally at the parietooccipital sulcus. The ventricle only showed a moderate extension, with no considerable hydrocephalus. Nothing particular was noticed microscopically. The case was interpreted as a pure innate hyperplasia, while headache and vomiting were attributed to the chronic meningitis. He dissociated his case of genuine hypertrophy—which in the past had only been described twice, once by Heinrich Obersteiner in Vienna and once by Paul Brouardel in Paris—from the cases of hyperplasia described by Rudolf Virchow in Berlin and by Carl von Rokitansky in Vienna; the latter cases were attributed to a selective proliferation of the glia.

In his second study, Tsiminakis histologically examined 26 cases of chronic internal hydrocephalus of inflammatory origin — the specimens having been provided by the pathologist Anton Weichselbaum (1845–1920) — and described the lesions in the ventricular ependyma and the choroid plexus that contributed to the genesis of the hydrocephalus. He found that the connective and perivascular tissues were richly infiltrated by cells, some of which were small round mononuclear cells, and others large, of an epithelial nature, with some evidence of proliferation [7, 8].

On a different subject, that of progressive paralysis, Tsiminakis ventured into an experimental treatment. He concluded [9] that the use of sodium nucleinate ($C_{47}H_{75}NO_{17}$ or ribonucleic acid sodium salt, classified as an immunomodulator today), which had been introduced by Julius Donath in Budapest in 1907 [10], should be taken into consideration. In 1912, apart from treatment with tuberculin or killed cultures of staphylococci and streptococci, one was almost powerless to combat tertiary syphilis. Although sodium nucleinate did not arrest the mental decay in all cases, the results of Tsiminakis in 15 patients suffering from progressive paralysis showed remissions and clinical improvement in several instances, thus suggesting value in sodium nucleinate treatment. His patients, all of whom showed a positive Wassermann reaction, were first given 3 injections of salvarsan at intervals of 8 days. Twenty days after the last injection of salvarsan, he began treatment with a 2% solution of sodium nucleinate in a 2% solution of sodium chloride, giving 8 injections at intervals of 7

days.

The topic of epilepsy, including post-encephalitic epilepsy, was a main focus of interest for Tsiminakis. By examining 8 patients, between 10 and 32 years of age, with inflamed tonsils and adenoids, Tsiminakis and his colleague, the otolaryngologist Athanasios A. Zografides (Fig. 2, left), defined a form of ‘reflex epilepsy’ (*Reflexepilepsie*) which receded following tonsillectomy [11, 12] (Fig. 2, right). The authors suggested that the prompt treatment of similar inflammatory conditions of the ear, nose, and throat during childhood is necessary in order to prevent reflex epilepsy from causing permanent brain damage and turning into true epilepsy.

His work on the compression of the carotids [13] to precipitate an epileptic convulsion, in order to differentially diagnose epilepsy from the simulation of epilepsy in hysterical conversion reactions (Fig. 1, right), received international recognition as the ‘Tsiminakis maneuver’ [14] or the ‘sign of Tsiminakis’ [15]. This phenomenon was subsequently confirmed by Julius Flesch [16] and by Paul Loewy [17].

As Kinnier Wilson [18] discussed, pressure on, or ligature of, the large arteries supplying the brain was known to provoke spasms since the early work of Sir Astley Paston Cooper, First Baronet [19]. Cooper occluded the carotid and vertebral arteries in a rabbit; spasms immediately resulted, and respiration ceased. In a dog, Cooper ligated the same four arteries; the animal recovered, following a preliminary stage of paralysis. Adolf Kussmaul and Adolf Tenner [20] tied the left subclavian and innominate arteries; the immediate symptoms were loss of consciousness and of voluntary movement, followed by clonic spasms (10–45 sec later) beginning in the muscles of the neck, dilatation of the pupils, respiratory gasps at longer intervals, and finally cessation of respiration. Moritz Schiff [21] and Leonard Hill [22] induced epileptiform clonic spasms in themselves by compressing one carotid artery. Following this, studies in cats and dogs were performed by the physiologist George N. Stewart in Chicago [23]. In addition, studies in normal and epileptic patients were performed by Tsiminakis in Athens [13]. The effects may vary in different persons owing to free anastomoses, but the inference that deficient blood supply could lead to unilateral or general fits, was regarded as established [18].

In the studies carried out by Tsiminakis [13], the carotids were compressed for 1 min in 30 healthy individuals, aged 18 to 30 years, and in 86 epileptic patients. In the control group, he did not observe any abnormal signs, apart from momentary unconsciousness. This momentary unconsciousness took longer than 30 sec to appear, and returned to the previous condition immediately after the pressure was relieved, without leaving any remnant of confusion, aside from a short duration of dizziness. Once the persons were unconscious, no convulsion was observed; however, complete relaxation of the entire muscular system was observed, with the head falling suddenly onto the shoulders and the body falling to the sides or the back. When he applied a similar pressure to the carotids of the epileptic group, they became unconscious more rapidly, after 30 sec at the most. The loss of consciousness was quickly followed by generalized epileptiform convulsions, in some of the patients, while the convulsions affected only one side of the body in others. In certain cases, a larger or

smaller portion of the facial muscles were involved. This state of convulsions lasted for approximately 10–40 sec, followed by confusion and the characteristic stare of vacant expression, as observed in many cases of attacks of epileptic somnambulism (*Absenz*). From a diagnostic point of view, he emphasized the value of his maneuver in differentiating true from simulated or feigned epilepsy, especially for forensic reasons or for soldiers enlisted in the army.

In reviewing chronic epilepsy, Tracy [24] argued that it is not merely a manifest diseased condition of the vegetative nervous system, particularly of the sympathetic nervous system, but it is also a condition of a hyperirritable cerebral cortex. Tracy based his arguments on the experiments of Tsiminakis [13, 25], who had shown that cortical cells, especially motor neurons, of the normal brain react to anemia differently than those of epileptics.

Tsiminakis [13] elaborated further on the pathogenesis of epilepsy in a series of papers and presentations at the Athens Medical Society, with reference to the historical literature on vasomotor disturbances in the brain, either as a cause of the epileptic paroxysm, a precursor of such an attack, or as a sequel thereof. Hughlings Jackson believed that, in most cases, the first functional alteration in epilepsy is of a circulatory nature, and that cellular excitability is the result of occlusion of very small arterial branches. Nothnagel suggested that the starting point for the loss of consciousness and convulsions is in the medulla and pons, and that during an epileptic attack the vasomotor center is stimulated, resulting in cerebral anemia. Bekhterev had concluded that the primary cause of an epileptic seizure is circulatory dysfunction of the brain resulting in the stimulation of its cortical centers.

In Athens, Tsiminakis [26] observed three cases of epilepsy following attacks of dengue at varying intervals, and compared them to similar cases that he had seen following encephalitis. His new patients were between 18 and 22 years of age, and none of them had any prior evidence of epileptic fits. The attacks commenced with giddiness and tremor of the entire body, followed by loss of consciousness and generalized muscle spasms; sleep followed. Upon awaking, the patients complained of headaches and extreme exhaustion. During the dengue epidemic in Athens, it was generally agreed that the virus was neurotropic, sometimes acting on the peripheral nervous system, and other times on the central nervous system.

Tsiminakis further reported on five cases of narcolepsy in patients aged 19 to 36 years, and discussed the condition in the context of previous contributions by Gélinau, Redlich, Economo, Kahler, Sommer, Mendel, Marburg, and Goldflam [27].

In 1935 he revisited the topic of epileptic convulsions, this time as a result of carotid aneurysms [28]. He reported on five cases (patients aged 35 to 65 years) of atherosclerotic aneurysms of one, or both, common carotid arteries, and the resulting circulatory disturbances of the brain. He also discussed previous interpretations by Hans von Haberer before the Vienna Medical Society in February 1918, and by Otto Foerster before the meeting of German Neurologists in September 1926.

At the Athens Medical Society, Tsiminakis regularly presented clinical reports, including

‘Fourteen cases of nervous system infections of unknown etiology’ (March 1923), ‘The use of serum derived from rabbits infected with herpetic encephalitis for the treatment of epidemic encephalitis’ (June 1923), ‘Six cases of epilepsy following epidemic encephalitis’ (March 1925), ‘Review of the malaria therapy of progressive paralysis and observations on 84 syphilis patients with other subsequent infections’ (May 1927), ‘Three cases of dengue epilepsy’ (December 1929), and ‘Four cases of narcolepsy’ (May 1930).

Legacy and Political Activity

Driven by his patriotic fervor, Tsiminakis postponed his studies in Vienna to volunteer as a Sanitary Warrant Officer in the Greco-Turkish War of 1897, serving in the hospitals of Volos, Larissa, Lamia, Styliis, and Hagia Marina. In 1912, he enlisted as a volunteer Captain Physician and marched into his native city of Kozani with the first army units [5]. He served again in 1915. Tsiminakis co-founded the ‘Panmacedonian Cause’ society in Athens, together with other famous Greeks, including the chemist Anastasios Christomanos (1841–1906), the statesman John Valalas (1875–1945), and the barrister Demetrius Dingas (1876–1974). During the Greco-Italian War of 1940–1941 Tsiminakis volunteered once again, serving as Captain Physician at the 8th Army Hospital of Athens.

In the national legislative election of December 16, 1923, Tsiminakis was elected—with the Liberal Party—a Plenipotentiary Member of Parliament of the Fourth National Assembly; he was sworn in on January 2, 1924 and served until September 30, 1925 [29, 30]. That period in Greek politics witnessed the succession of seven governments, including the one headed by Prime Minister Alexandros Papanastasiou (1876–1936) from March 12, 1924, to July 24, 1924. On March 25, 1924, Papanastasiou (a politician highly educated and with an unusual ethos) proclaimed the Second Hellenic Republic, a regime of Parliamentary Republic (which lasted until 1935), following the Constitutional Monarchy of 1862–1924. On June 14, 1925, Papanastasiou founded the Aristotelian University of Thessaloniki, the largest University in Greece today. In his will, Papanastasiou left his brain to Koskinas, who recorded its weight (1387 g) in the entry on ‘the brain’ that he contributed to the ‘Helios Encyclopedia’ [4].

In terms of personality, Tsiminakis was described as defending his scientific views rigorously but graciously, without rushing to reject views opposing his own [5]. He was a vivid orator and a talented poet, often opening friendly discussions with lyrical verses.

In a lecture delivered in 1934 before the Parnassus Literary Society, under the title ‘Are Freud’s claims on artistic creativity founded?’ (Fig. 3), he took a negative stance toward the psychoanalytic interpretation of art and artists, using as examples artists, poets, and playwrights, such as Leonardo, Michelangelo, Shakespeare, El Greco, Lord Byron, Baudelaire, Victor Hugo, Richard Wagner, Théophile Gautier, and Leconte de Lisle, as well as the Greek poets Palamas, Drosinis, Melas, and Crystallis. Commenting on Freud’s study *Der Dichter und das Phantasieren* (1907/1908), Tsiminakis rebutted the doctrine of a ‘vague’ unconscious, dominated by unfulfilled sexual desires, and the origin

of artistic creation and poetic inspiration in emotivity, rooted in the subconscious. He argued that ‘psychoanalytic ideas are neither based on scientific observations nor on true research, but rather, on dialectics and delirium’. He cited Oswald Bumke, who had remarked that ‘psychoanalysis lacks any sort of proof, being instead a sophism, not a natural science in the eyes of anyone requiring evidence from any research, not even a science’. Instead, Tsiminakis proposed that art is a deliberate act, underpinned by cerebral physiology; a balance of logic and emotions, based on the sense of beauty in the artist’s mind, who creates under special circumstances of inspiration. Artistic creation and artistic genius stem from the intellect, which is moulded by education and a favorable environment, with constant mental work and observation. In December 1936, he delivered another lecture before the same society, on ‘The influence of nature on emotions and the mind’.

His son, Yanni Tsiminakis (1906–1977), graduated in medicine from Vienna University in 1928, and worked at the Neurological Institute under Otto Marburg (1874–1948), and at the Psychiatric Clinic under Otto Pötzl (1877–1962). In 1933 he joined the faculty of the Department of Neurology and Psychiatry of the University of Athens [2].

A street is named after Constantin Tsiminakis in his native Kozani.

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Disclosure Statement

The author reports no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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Figure captions

Fig. 1. Left, Constantin J. Tsiminakis. Credit: Helios Encyclopedical Lexicon [2]. Right, offprint of his original paper describing the carotid compression which later became known as the ‘Tsiminakis maneuver’ [13]. Credit: National Library of Greece, Athens (call number IAT2583OK.1944).

Fig. 2. Left, Athanasios A. Zografides, born in 1880, who also originated from Kozani. He was a respected ear, nose, and throat specialist and a philanthropist. After graduating in medicine from the University of Athens in 1901, he trained in Odessa, Moscow, and Vienna [12]. Right, title page of the publication co-authored by Tsiminakis and Zografides on ‘The etiology and treatment of epilepsy’ [11]. Credit: Bavarian State Library, Munich.

Fig. 3. Tsiminakis’ monograph on ‘Freud and artistic creativity’ published in 1934 in Athens by the I. L. Alevropoulos Company (author’s archive).