von Economo, Constantin

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Constantin von Economo (1876-1931)

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The following article is based on the biographical note of Constantin von Economo published by the author in Appendix I of the first English edition of the Economo and Koskinas *Atlas of Cytoarchitectonics of the Adult Human Cerebral Cortex*, Karger, Basel (2008), as well as the papers on the life and work of Economo and Koskinas published in *Brain Research Bulletin* (Triarhou 2005, 2006b, 2006c), *Journal of Neurology* (Triarhou 2006a, 2007c), and *Stereotactic and Functional Neurosurgery* (Triarhou 2007a, 2007b).

Constantin von Economo (Figure 1) was born on 21 August 1876 in Brăila, Romania (Figure 2). He was the fifth child, among two daughters and five sons, of Johannes and Hélène Economo (née Murati). The two families were rooted in the Hellenic region of Macedonia (in the cities of Edessa and Serres, respectively). Johannes Economo had left Greece for France during the Ottoman rule of northern Greece; the Murati family had left Greece for Budapest in the 1820s. The Economo family had taken up citizenship in the Austro-Hungarian Empire shortly before World War I and belonged to a group of respected families of Greek origin with such names as Karajan, Ypsilanti, Dumbas and Christomano. Johannes was made Imperial Baron (Freiherr) in 1904.

Figure 1: Constantin Freiherr von Economo (1876-1931). Photo by Max Schneider, Vienna.

In 1877, a year after the birth of Constantin, the Economo family moved to Trieste, where he

grew up and attended school. He was fluent in Greek, German, French, Italian and English. He began his studies in 1893 with two years of mechanical engineering at Vienna's Polytechnic (Technische Hochschule Wien), switching to medicine in 1895 at the University of Vienna (Figure 3), graduating in 1901. Economo stayed one more year in Vienna to train in internal medicine under Hermann Nothnagel. In 1903 he went to Paris for a year, to train in psychiatry with Alexis Joffroy and Valentin Magnan and at the neurological service of La Salpêtrière under Pierre Marie and Fulgence Raymond. During that time, Economo must have crossed in his training path with Cajal's associate Nicolás Achúcarro (1880-1918), who was also studying with Marie in France and with Kraepelin and Alzheimer in Germany between 1904 and 1908. Economo next spent three months in Strassburg, training in anatomy with Albrecht von Bethe and physiology with Julius Ewald. Next he visited the psychiatric clinic of Emil Kraepelin in Munich, where he worked for six months in neurohistology under the supervision of Alois Alzheimer, and then Berlin, where he worked in neurology with Hermann Oppenheim and psychiatry with Theodor Ziehen. He concluded his study trip with a visit to the Zoological Experimental Station at Trieste working on comparative neuroanatomy with Carl Isidor Cori.

Figure 2: Economo's birthplace, the coastal city of Brăila in Romania. From a period postcard.

Economo made his scientific début with a histological study on the embryonic development of the pigeon and chick hypophysis, published in Vienna's Proceedings of the Imperial Academy of Sciences (Economo 1899). In a subsequent work, carried out in Munich under Alzheimer's supervision under the title 'Contributions to the normal anatomy of ganglion cells', he firmly supported Cajal's neuronism (Economo 1906).

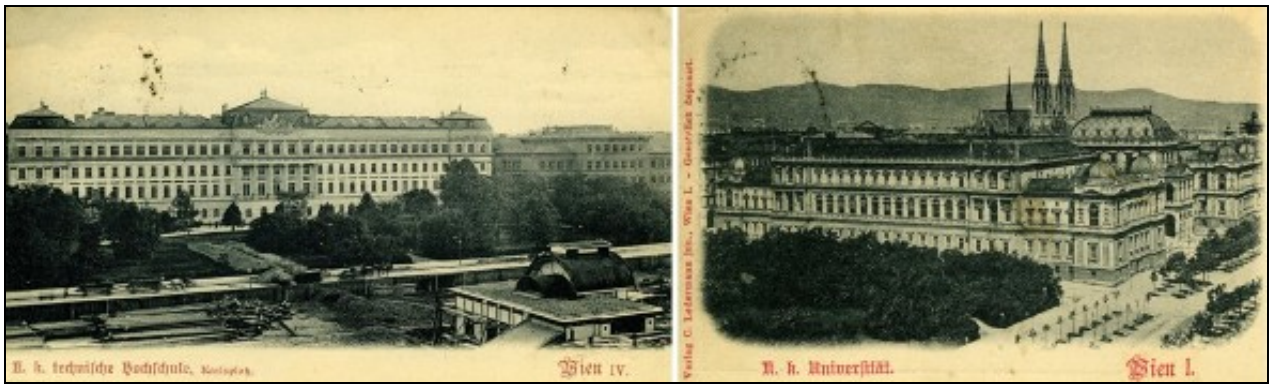


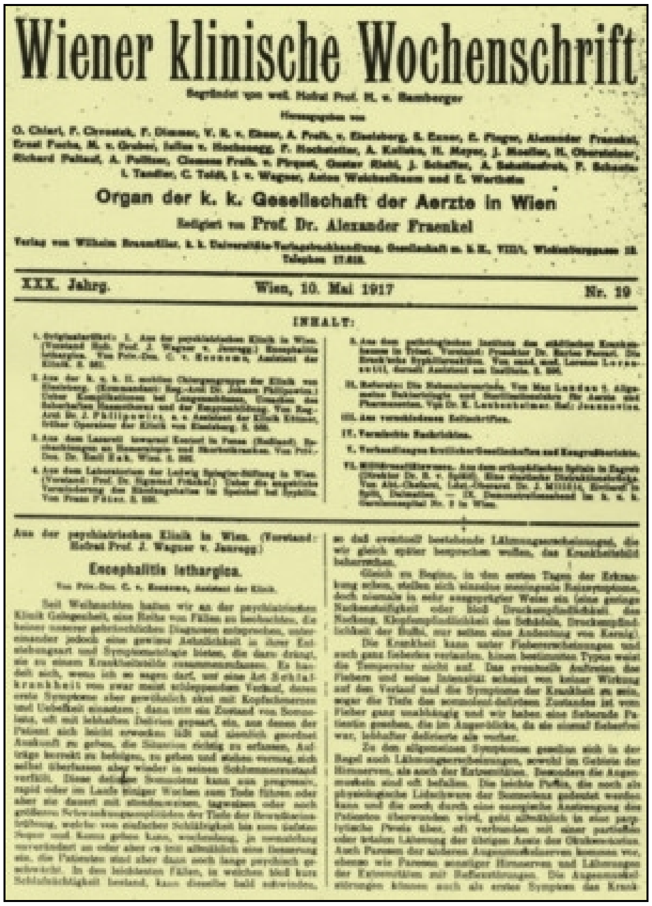
Figure 3: The Technical University of Vienna (left) where Economo began his studies, and the

University of Vienna (right), where he moved after two years to study medicine. From period postcards.

On 1 October 1906, Economo became an assistant at the Clinic for Psychiatry and Nervous Diseases headed by Julius Wagner von Jauregg at Vienna's General Hospital. Economo's (1911) Dozentenarbeit (thesis) was 'On the dissociated sensory disturbances accompanying pontine tumors, and on the central tracts of the sensory trigeminal.' Between 1909 and 1920, he published articles on posthemiplegic chorea, Wilson's disease (Economo 1918), optic neuritis, multiple sclerosis, progressive paralysis, head injuries, presenile disease, and the heritability of mental traits. Economo was appointed Lecturer at the University of Vienna in 1913 and Professor of Neurology and Psychiatry in 1921. During World War I, Economo served at the Russian front and on the South Tyrol front as a pilot. In 1916 he was summoned back to the Vienna Hospital as a military physician to attend to patients with head injuries.

In 1907 Economo became interested in aeronautics, initially flying balloons. He was the first Austrian citizen to obtain an international pilot's licence and among the first pilots to fly at the Wiener-Neustadt field. In recognition of his instruction services, he was given Field-Pilot's Certificate No. 1 by the Austro-Hungarian military aviation in 1912. Later on he received the Iron Cross for his contribution to the development of Austrian aviation. He was elected President of the Austrian Aëro-Club in 1910, an office he held for 16 years.

On 17 April 1917, Economo defined and presented epidemic encephalitis lethargica (known since as 'von Economo disease') to the Viennese Society for Psychiatry and Neurology (Economo 1917a, 1917b, 1920). His initial presentation was published in the 10 May 1917 issue of *Wiener Klinische Wochenschrift* (Figure 4). He published two monographs on encephalitis lethargica (1917c, 1929a), documenting its neuropathological basis and full clinical spectrum (somnolent-ophthalmoplegic, hyperkinetic, and amyostatic-akinetic forms). Encephalitis lethargica occurred worldwide in 1915-27 and was a major cause of post-encephalitic Parkinsonism. Economo described substantia nigra lesions in the chronic form in 1919, pinpointing the importance of this nucleus for extrapyramidal syndromes in the same year that Trétjakoff independently described nigral degeneration as the neuropathological hallmark of Parkinson's disease. Economo distinguished encephalitis lethargica from hemorrhagic encephalitis and the 1918-19 Spanish flu and from other epidemic encephalitides of the late 1920s. He reviewed these in a 1931 presentation (his last) at the First International Neurological Congress in Berne. The studies of Economo on encephalitis lethargica continue to exert a high impact to this day.



Wiener klinische Wochenschrift

Organ der k. k. Gesellschaft der Aerzte in Wien

Redigiert von Prof. Dr. Alexander Fraenkel

XXX. Jahrg. Wien, 10. Mai 1917 Nr. 19

INHALT:

Encephalitis lethargica.

Figure 4: Frontispiece of the original publication of Economo (1917) where he described encephalitis lethargica for the first time.

The pathoanatomical study of brain specimens from patients who had died of encephalitis lethargica offered Economo an opportunity to probe into the function of sleep (1925a, 1929b). The frequent occurrence of pathologically increased sleep in encephalitis lethargica and the varied ways in which sleep function may be otherwise disturbed prompted him to assume that rostrally from the nucleus of the third cranial nerve, in the transitional parts of mesencephalon to diencephalon, there must actually be gray masses that exercise a primary influence on the induction and course of sleep. He postulated the existence of an active sleep-regulating mechanism in 1918 and localized it with probability by clinical observations from 1923 to 1925 (Figure 5).

In a lecture delivered to the Society of Physicians in Vienna in March 1925, he highlighted the periodicity of sleep and wakefulness. He underlined that sleep and wakefulness have not only quantitative, but also qualitative differences, and suggested the active and reversible function of a 'sleep-regulatory center' located near the oculomotor nucleus, the aqueduct of the third ventricle and the infundibular region, in the vicinity of other important vegetative centers regulating temperature, salt and water metabolism (Figure 5). In 1929 he gave a presentation on sleep at the College of Physicians and Surgeons of Columbia University (Economo 1930a). The concepts of Economo on sleep regulation anticipated some of the current theories on sleep: advances in brain research in the 1990s confirmed his remarkable predictions.

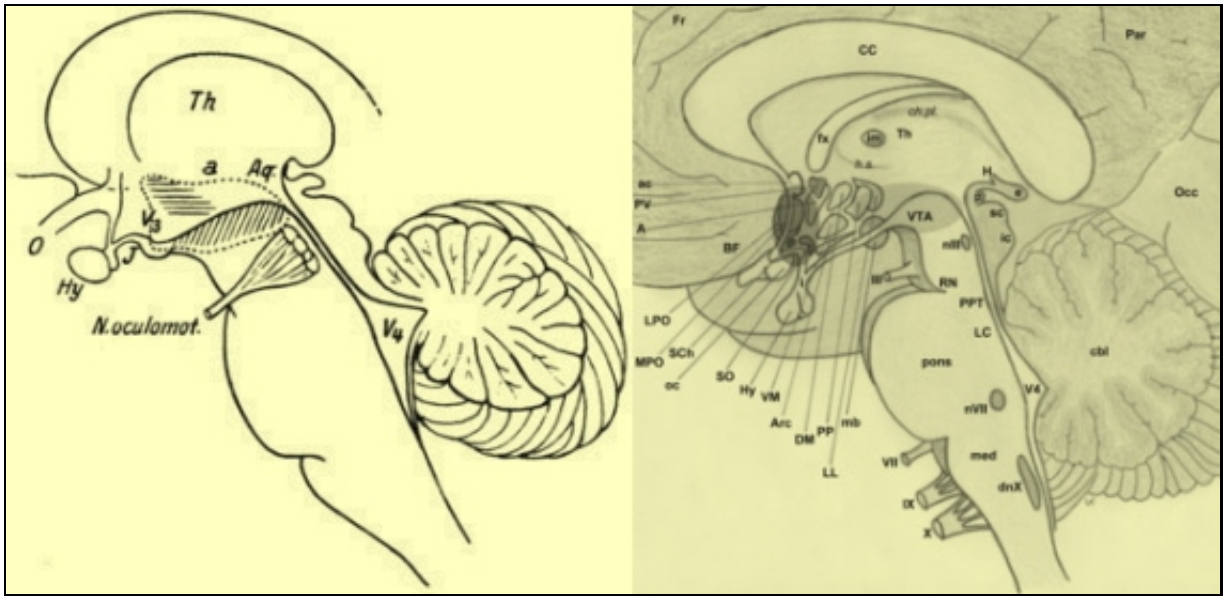


Figure 5: Left: Economo's marking of the boundary (dotted line a) of the field in the diencephalic-mesencephalic transition, in which the center for the brain regulation of sleep lies. Lesions in the anterior, 'sleep' part (horizontal lines) cause insomnia; lesions in the posterior, 'waking' part (slant lines) induce sleep. Aq, aqueduct; Hy, hypophysis; J, infundibulum; O, optic chiasm; Th, optical thalamus; V3, third ventricle; V4, fourth ventricle (Economo 1925a). Right: A modern anatomical drawing of the medial aspect of the human brain, outlining the topography of regions that Economo defined as being involved in sleep regulation on the basis of his histopathological observations. The predicted 'sleep part' is indicated by a vertically-oriented, dark-grey ellipse; the 'waking part', by a horizontally-oriented, light-grey ellipse. CC, corpus callosum; Fr, Par, Occ, frontal, parietal & occipital lobes; cbl, cerebellum; fx, fornix; Th, thalamus; im, intermediate mass of thalamus; ch. pl., choroid plexus of third ventricle; h.s., hypothalamic sulcus; H, habenula; e, epiphysis; ac, p, anterior & posterior commissure; oc, optic chiasma; Hy, hypophysis; i, infundibulum; mb, mamillary body; sc, ic, superior & inferior colliculus; III, VII, IX, X, cranial nerves; dnX, dorsal nucleus of X; BF, basal forebrain; VTA, ventral tegmental area; RN, raphé nuclei; PPT, pedunculopontine tegmental nuclei; LC, locus coeruleus; med, medulla oblongata; V4, fourth ventricle. Hypothalamic nuclei: PV, paraventricular; A, anterior; LPO, lateral preoptic; MPO, medial preoptic; SCh, suprachiasmatic; SO, supraoptic; VM, ventromedial; Arc, arcuate; DM, dorsomedial; PP, posterior hypothalamic area/posterior level; LL, lateral hypothalamic area/lateral level (Triarhou 2006c).

In 1925 he published in German, together with Georg N. Koskinas (1885-1975), the monumental *Atlas of Cytoarchitectonics of the Adult Human Cerebral Cortex* (Figure 6), defining five structural cortical types (Economo 1925b, 1927, Economo and Horn, 1930) – agranular, frontal, parietal, polar and koniocortex (Figure 7) – and, on that basis, the 107 Economo-Koskinas modification areas (22 allocortical, 22 heterotypic isocortical and 63 homotypic isocortical) in the human cerebral cortex (Figure 8). These were histologically documented in 112 brilliant microphotographic plates 48×48 cm in dimension (Economo and Koskinas 1925, 2008). The work took the field of cortical cytoarchitectonics to a new zenith, following the tradition of Berlin anatomist Korbinian Brodmann (1868-1918) who, 16 years earlier, had published the monograph in which he had developed his own division of the cerebral cortex into 52 discrete areas (of which 44 areas for the human cerebral hemispheres). Economo and Koskinas devised a unique method of perpendicular sections for each gyral segment, essentially providing a virtual 'flattening-out' of the entire cerebral mantle and thus bypassing the problem of macroscopically extrapolating Brodmann projection maps as a 'shorthand system' to designate regions on the cerebral surface, something commonly done today; they critically compared their 107 cortical subdivisions with Brodmann areas, as well as those of all preceding investigators, all the way to Viennese psychiatrist Theodor Meynert (1833-92) who is generally credited with the birth of the field of cortical architectonics in 1867.

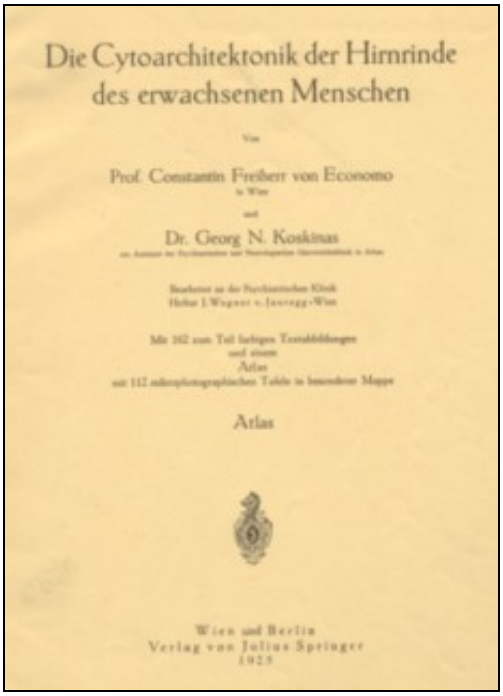


Figure 6: Frontispiece of the booklet that accompanied the Economo and Koskinas (1925) *Atlas of Cytoarchitectonics*.

In the last four years of his life, Economo became increasingly interested in evolutionary neuroanatomy and its relation to the substrate of human culture. He advanced propositions on intelligence and the future evolution of the human brain. He postulated a principle of 'progressive cerebration' to connote the phylogenetic increase in brain size, coupled with the progressive cytoarchitectonic differentiation of newly acquired brain structures and their increasing specificity, and the mind's constant evolution through the generations, especially in the prefrontal and parieto-temporal cortices. He maintained that in the course of thousands of centuries, the human brain may develop yet unimagined mental capabilities (a circumstance opening up totally new perspectives for the evolution of mankind), and considered that a glimpse into that future might be caught by studying the 'élite brains' of the gifted and talented (Economo 1928, 1929c, 1930b, 1930c, 1931a).

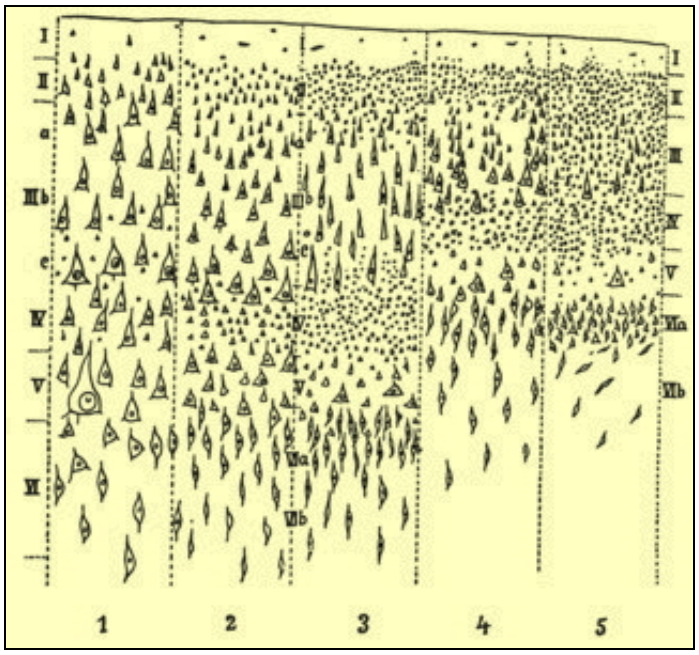


Figure 7: The five structural types of cerebral cortex described by Economo (1925b) and Economo

and Koskinas (1925, 2008). Types: 1, agranular; 2, frontal; 3, parietal; 4, polar; 5, granular (koniocortex).

On 7 May 1931, Economo inaugurated the new Brain Research Institute in Vienna as its first director. In his opening address, entitled 'Problems of Brain Research,' Economo (1931b) announced an ambitious and extensively planned program to further study the fine anatomical structure of cortical cells and fibers, individual variations in cortical structure, hemispheric asymmetry, sexual dimorphism, human brain development and aging, cytoarchitectonics in neuropathology, comparative and evolutionary neuroanatomy at the interface with anthropology, the neuroanatomy of the gifted and talented, and the genetics of brain disorders. From August 31 until September 4, he attended the First International Neurological Congress at Berne, which he had been instrumental in organizing; he gave a lecture on encephalitis japonica and the non-suppurative encephalitides.

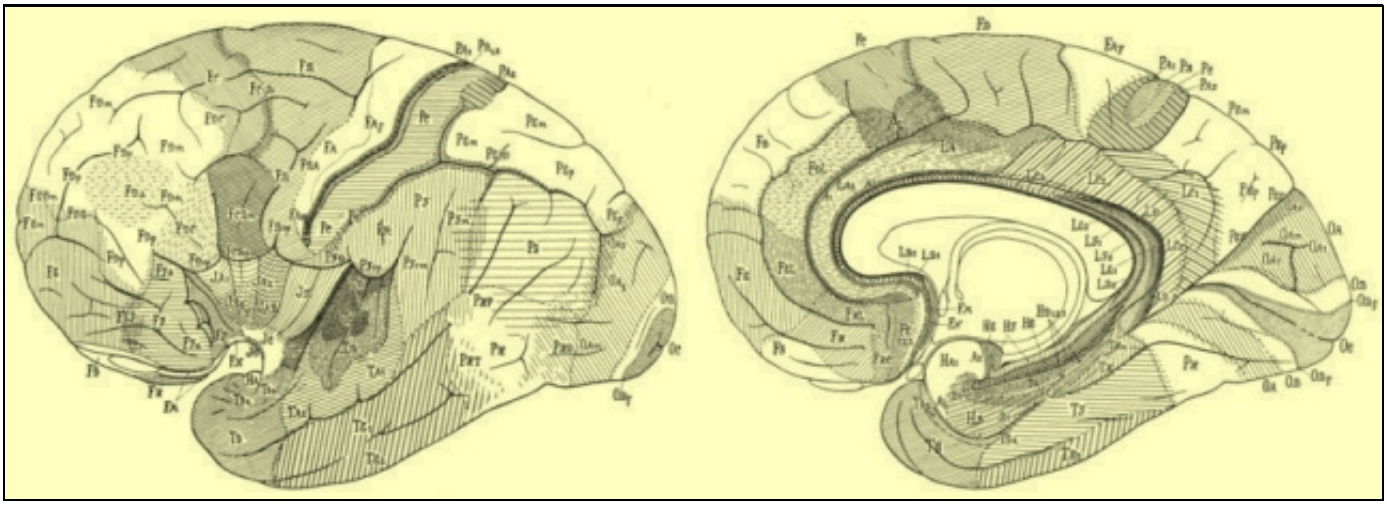


Figure 8: Lateral (left) and medial views (right) of the human cerebral hemispheres with the nomenclature of Economo and Koskinas (1925, 2008) defining their 107 cortical cytoarchitectonic modification areas.

Constantin von Economo left marks of brilliance on neuroscience, documented in a record of 166 published items (archived in Appendix II of the *Atlas*), produced over a 33-year period and amounting to some 4200 pages. He also kept a life-long interest in international neurology, the relation of neurology to general medicine and psychiatry, and the promotion of neurosurgery as an independent medical discipline. Stransky calls Economo "a gentleman of the old school" and Seitelberger characterizes him as "the greatest Austrian neuroscientist." He is described as a fine character, a scientist in the best sense of the word, and peerless as a man, a "gentleman of the old school." Wagner von Jauregg wrote that "Economo's merits were patience, perseverence, thoroughness, exactness, industry to the highest degree, adherence to plan, complete mastery of technique, correct evaluation of the data, and rigid logic in drawing conclusions; absolute dependability; bridled imagination, routed into the proper path through the critical quality; veracity and sober objectivity; complete devotion to the idea the realisation of which occupied him."

In Vienna, Economo lived at Rathausstrasse 13 from 1906 until the end of his life; a plaque reminds today's visitor that "Constantin von Economo the great brain researcher and friend of mankind lived in this house" (Figure 9, left and centre top). He was married to Princess Karoline von Schönburg-Hartenstein (1892-1986). He died on 21 October 1931 in Vienna. For his research on the brain, Constantin von Economo won the 1928 'Aristeion of Science' award from the Academy of Athens. He was nominated for the 1926, 1930 and 1932 Nobel Prize in Physiology or Medicine for his work on encephalitis lethargica. In 1976, he was honoured by the Austrian Government with a portrait stamp issued on the centennial of his birth (Figure 9, centre bottom). A marble bust of Economo, made by artist Max Kremser based on a Poller cast, decorates the Arkadenhof at the University of Vienna, in the company of Theodor Meynert, Hermann Nothnagel, Heinrich Obersteiner, Erwin Schrödinger and other eminent professors of the prestigious institute (Figure 9,

right).

Figure 9: The entrance to Economo's house on Rathausstrasse 13, Vienna (left) and the commemorative plaque (center top). The Austrian stamp issued on the centennial of his birth in 1976 (center bottom) and the marble bust decorating the Arkadenhof of the University of Vienna (right). Photos by the author.

An annotated registry of the complete published works of Constantin von Economo can be found in Appendix II of the English edition of the *Atlas of Cytoarchitectonics* (Economo and Koskinas 2008).

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Favourite Sentences

On the interdisciplinarity of sciences:

"What we group under the name of the sciences is, as the application of the word in the plural shows, no single entity, but consists of many separate fields of knowledge, which often lie far apart. Through the increase of such knowledge, these fields increase, and their boundaries, originally far apart, approach each other more and more. The investigation of these border zones then becomes one of the most interesting problems in science and a new branch of science itself, whereby the experience and methods of one speciality are applied to the other and entirely new points of view are reached that lead to fruitful work in both fields."

On human achievements in relation to brain evolution:

"God, or nature, or whatever else you wish to call the mysterious creative force of this world, which in the course of millions of years on the long scale of phylogenetic development has shaped out of the simple cell all the diverse and ever more complex varieties of life, has, of all living beings on this earth, endowed only the human species with the capacity to create new things. Creation has impressed a part of its own creative craft upon the brain of humans, enabling them to create anew. It is this same force of nature, which in the course of eons gave the eagle its flight, that in recent decades has enabled us humans based on our knowledge to construct wings and overcome the ties of gravity that bind us to the Earth."

On human flight:

"Calculation shows that to lift or project a body to space beyond the gravitational pull of our Earth, it would require a terrific amount of explosive material, several thousand times the mass of the body in question. Yet modern physics research shows that once we have a means of mastering the disintegration of atoms, which has been shown to be possible, and make that energy utilizable, a force will be at our disposal to transcend the force of gravity. Those who then as worthy sons of the Titans make these first journeys will be of the same stuff as their predecessors who conquered the air, and from the ranks of the conquerors of the air will advance these stormers of the heavens."

On the neuroanatomical basis of psychology:

"Encephalitis lethargica has fundamentally influenced our appreciation of normal and pathological psychological manifestations. The dialectic combinations and psychological constructions of many ideologists will collapse like houses of cards if they do not in the future take into account these new basic facts. Every psychologist who in the future attempts to deal with psychological phenomena such as will, temperament, and fundamentals of character, such as self-consciousness, the 'ego', etc., and is not well acquainted with the appropriate observations on encephalitis patients, will build on sand. Many an elaborate constructions of the purely speculative psychologists will be dashed to the ground in the face of these everyday facts of the physician. It is to be hoped that this will not merely furnish the theorists with one reason more for avoiding these facts. Encephalitis lethargica can scarcely again be forgotten."