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# Cytoarchitectonics of the Human Cerebral Cortex: The 1926 Presentation by Georg N. Koskinas (1885–1975) to the Athens Medical Society

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## 1. Introduction

The Greek neurologist-psychiatrist Georg N. Koskinas (1885–1975) is better known for his collaboration with Constantin von Economo (1876–1931) on the cytoarchitectonic study of the human cerebral cortex (von Economo & Koskinas, 1925, 2008). Koskinas seems to have been one of those classically unrecognised and unrewarded figures of science (Jones, 2008, 2010). Such an injustice has been remedied in part in recent years (Triarhou, 2005, 2006). The



Fig. 1. The Vienna General Hospital on the left, where Koskinas worked between 1916 and 1927 under the supervision of Julius Wagner von Jauregg (1857–1940) and Ernst Sträussler (1872–1959) (author’s archive). The 1926 roster of the Vienna Society for Psychiatry and Neurology on the right, showing Koskinas as a regular member (Hartmann et al., 1926)

year 2010 has marked the 125th birthday anniversary of Koskinas (1 December 1885) and the centennial of his graduation from the University of Athens (M.D., 1910).

As soon as the Atlas and Textbook of Cytoarchitectonics were published in 1925, Koskinas briefly returned to Greece and donated a set to the Athens Medical Society. On that occasion, he delivered a keynote address, which summarises the main points of his research with von Economo. That address (Koskinas, 1926) forms the main focus of this paper. There are only two other presentations known to have been made by Koskinas: one with von Economo at the Society for Psychiatry and Neurology in Vienna in February 1923 (von Economo & Koskinas, 1923), presenting an initial summary of cytoarchitectonic findings on the granularity of sensory cortical areas especially in layers II and IV; and the other with Sträussler at the 88th Meeting of the German Natural Scientists and Physicians in Innsbruck in September 1924 (Sträussler & Koskinas, 1925), reporting histopathological findings on the experimental malaria treatment of patients with general paralysis from neurosyphilis.

## 2. The 1926 presentation by Koskinas

The following is an exact English translation of the *Proceedings* of the Athens Medical Society, Session of Saturday, 23 January 1926, rendered from the original Greek text (Koskinas, 1926) by the author of the present chapter.

### 2.1 Introductory comment by Constantin Mermingas, presiding

"I am in the gratifying position of announcing an exceptional donation, made to the Society by the colleague Dr. G. Koskinas, sojourning in Athens; having temporarily come from Vienna, he brought with him a copy, as voluminous as you see, but also as valuable, of the truly monumental compilation, produced by the two Hellenic scientists in Vienna, C. Economo and G. Koskinas, who is among us today. It involves the book—text volume and atlas—*Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*, about the value of which we had learnt from reviews published in foreign journals, but also convinced directly. Dr. Koskinas deserves our warm thanks, as well as our gratitude, for being willing to deliver a synopsis of that original scientific research and achievement."

### 2.2 Main lecture by Georg N. Koskinas, keynote speaker

"Thanks to the ardour of the honourable President of the Society, Professor Dr. Mermingas, who is meritoriously making every attempt to highlight the Society as a centre of noble emulation in scientific research and the promotion of science and at the encouragement of whom I have the honour of being a guest at the Society today. Enchanted by that, I owe acknowledgments because you are offering me the opportunity to briefly occupy you in person about the work published by Professor von Economo and myself in German, and deposited to the chair of the Society, "The Cytoarchitectonics of the Human Cerebral Cortex" (*Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*). An attempt on my behalf to analyse that work requires much time and many auxiliary media which, simply hither passing through, I lack. That is why I wish to confine myself, such that I very briefly cover the following simply and to the extent possible.

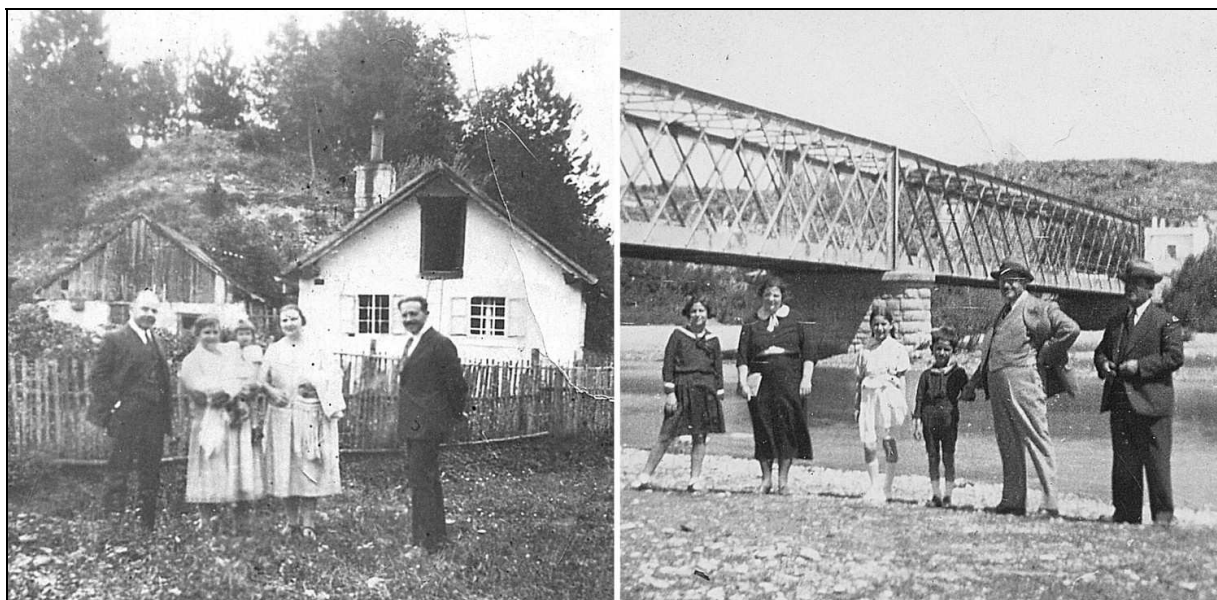


Fig. 2. Previously unpublished photographs of Koskinas and family members. The left photograph, taken in Vienna around 1926, shows Koskinas (first from the right) with his wife Stefanie, their daughter, his sister Paraskevi and her husband. The right photograph shows Koskinas (second from the right) in the Peloponnese in the 1940s – the bridge of the Eurotas River appears in the background – with his wife and daughter (left), and the children of his sister Irene and their father (photos courtesy of Rena Kostopoulou)

### 2.2.1 Incentives and aim

The incomplete and largely imperfect knowledge of the histological structure of the brain constituted the main reason that led us to its detailed architectonic research, and its ultimate goal was the localisation, to the extent possible, of the various cerebral functions and the pathological changes in mental disorders, as well as the interpretation of numerous problems, such as individual mental attributes, i.e. the talent in mathematics, music, rhetoric, etc.

### 2.2.2 Methods

At the outset of our studies we came across various obstacles and difficulties deriving on one hand from the very structure of the brain and on the other from the deficiency of the hitherto available research means. That is why we were obliged to modify numerous of the known means, to incise absolutely new paths, taking advantage of any possible means towards a precise, reliable and indelible rendition of nature. We modelled an entire system of new methods of brain research from the autopsy to the definitive photographic documentation of the preparations. Thus, we were able to not only solve many of the problems, but also, and above all, to provide to anyone interested various topics for investigation, as well as the manner for exploring them.

Allow me to mention some of the employed research means.

*Sectioning method.* Instead of the hitherto used method of sectioning the whole brain serially perpendicular to its fronto-occipital axis (Fig. 5), whereby gyri are rarely sectioned perpendicularly, we effected the sections always perpendicular to the surface of each gyrus and in directions corresponding to their convoluted pattern (Fig. 6). We arrived at that act



by the idea that, in order to compare various parts of the brain cytoarchitectonically, sections must be oriented perpendicularly to the surface of the gyri, insofar as only then is provided precisely the breadth of both the overall cerebral cortex and of each cortical layer.

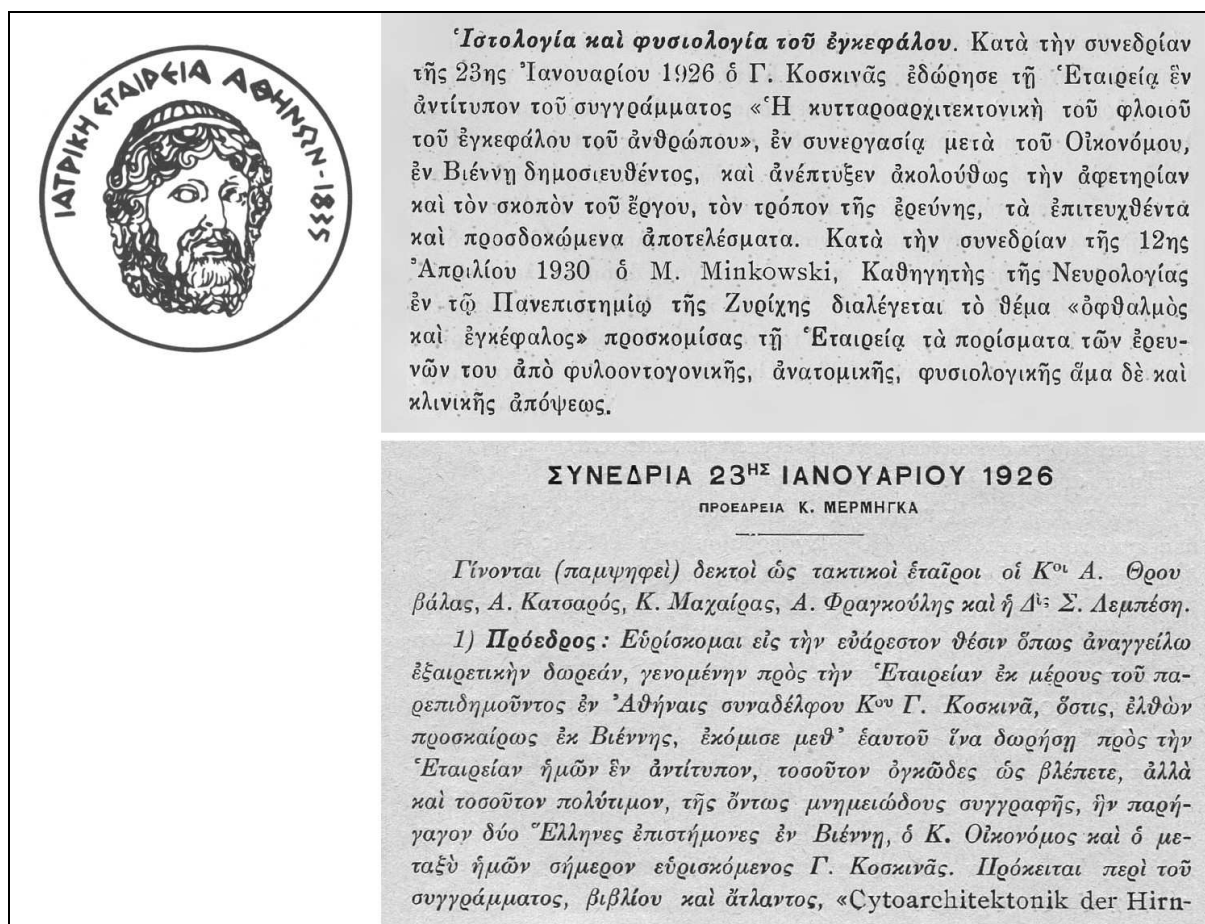


Fig. 3. The Proceedings of the Athens Medical Society for the Session of 23 January 1926

*Staining method.* The staining of the preparations was perfected by us such that a uniform tone was achieved not only of a single section, but of all the countless series of sections into which each brain was cut for study. And that was absolutely mandatory, on one hand in order to define the gradual differences of the histological elements of the neighbouring areas of the cerebral cortex, and on the other hand to achieve a consistent photographic representation.

*Specimen depiction method.* The hitherto occasional histological investigations of the brain depicted things schematically and therefore subjectively. Instead of such a schematic depiction, aiming at a precise representation of the preparations with all the relationships of the countless and polymorphous cells, we used photography. Photographic documentation constitutes the most truthful testimony of the exact depiction of nature, providing truly objective images of things as they bear in natural form, size and arrangement (Fig. 7). But to succeed in the photographic method it became necessary to turn to the study of branches foreign to medicine, such as advanced optics and photochemistry. We took advantage of both of these as much as we could. Lenses, light beams, filters, photographic plates and finally the photographic paper itself were all adopted towards the accomplishment of the intended goal of the most perfect, i.e. the photographic, depiction.



Fig. 4. Constantin Mermingas (1874–1942), Professor of Surgery at the University of Athens and President of the Athens Medical Society (left), Georg N. Koskinas (1885–1975) in the centre, and Spyridon Dontas (1878–1958), Professor of Physiology and Pharmacology at the University of Athens and President of the Academy of Athens (right). © 1957 *Helios Encyclopaedical Lexicon* (signatures from the author's archive)

### 2.2.3 Accomplished and anticipated results

Through our work an extremely precise and detailed description was achieved of the normal histological structure of the cerebral cortex as it is depicted in the photographic plates and explained in the text. Our photographic plates in the atlas, as such, constitute an ageless, imprescriptible opus, the basis and the control of any future research on the cerebral cortex. Whatever in such research is in agreement with the plates, must be considered as normal, and whatever diverges constitutes a pathological condition. From that precise knowledge of the architectonic structure of the cerebral cortex, which we achieved, it is allowable to anticipate the solution of numerous and different questions and issues of utmost importance; from their endless number I suffice in mentioning e.g. the following.

- a. *The problem of problems, i.e. the problem of the psyche.* When, as anatomists and physiologists, we speak of the psyche, we do not refer to it as a metaphysical being that finds itself a priori outside any anatomical and physiological weight, but as a moral, mental, active and historical personality which interacts with others and influences ourselves.
- b. *The problem of individual mental attributes, i.e. intellectual talents,* such as rhetoric, music, mathematics, delinquency and the variations in the mental development of human phyla on the earth. By comparing e.g. the centres of music in individuals who genetically present a total lack of music perception to individuals who possess an evolved musical talent we may exactly pinpoint differences in such music centres.



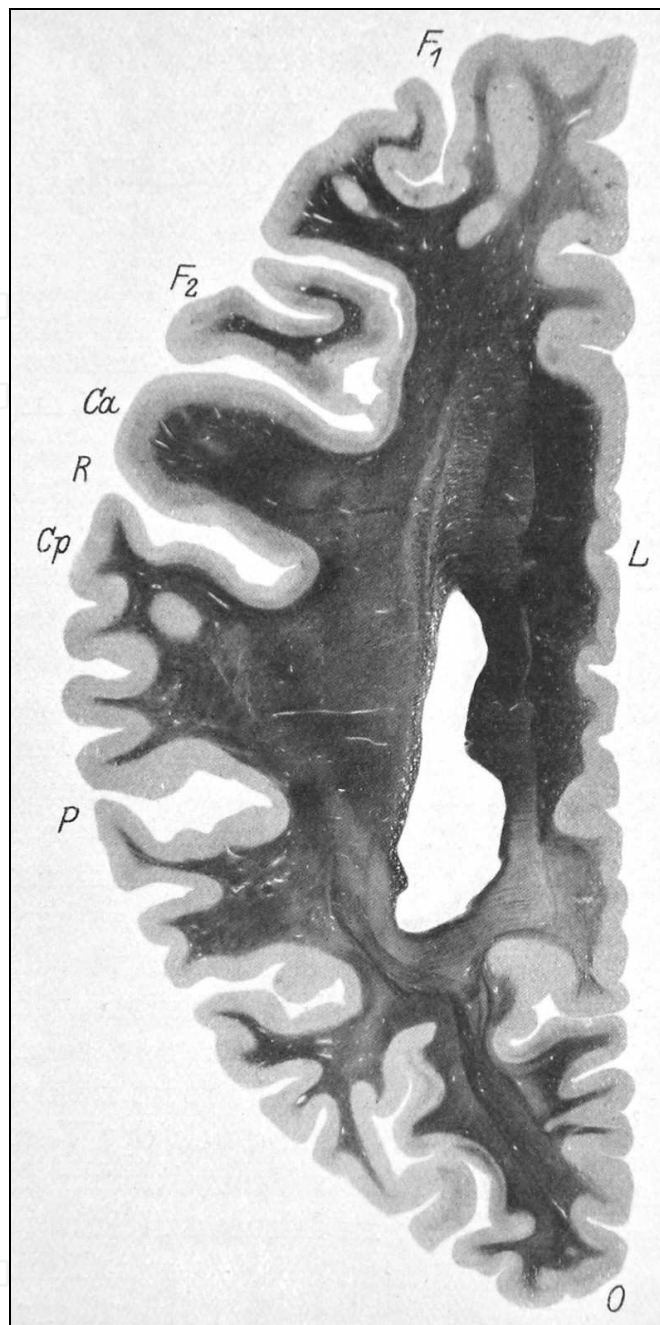


Fig. 5. Horizontal section through the left human cerebral hemisphere, depicting the sizeable regional differences in cortical thickness and the random orientation of the gyri (Koskinas, 2009). Weigert method.  $F_1$  and  $F_2$ , superior and middle frontal gyrus;  $Ca$ , precentral gyrus;  $R$ , central sulcus;  $Cp$ , postcentral gyrus;  $P$ , parietal lobe;  $O$ , occipital lobe;  $L$ , limbic gyrus

- c. *The problem of pathological lesions in numerous mental disorders* both primarily and secondarily encountered in the brain.
- d. *The problem of the localisation of various centres.* The various localisations of sensation, movement, stereognosis, speech, etc., which thus far were mostly defined without an exact histological control, from now on, admittedly, can be readily and precisely defined on the basis of the cerebral cortical areas that we have designated, which from a total number of 52 known thus far we brought to 107 (Fig. 8–10). The solution of this

problem also possesses utmost sense, insofar as in that way diagnosis can be readily effected, foci can be defined with precision and brain surgery can be enhanced.

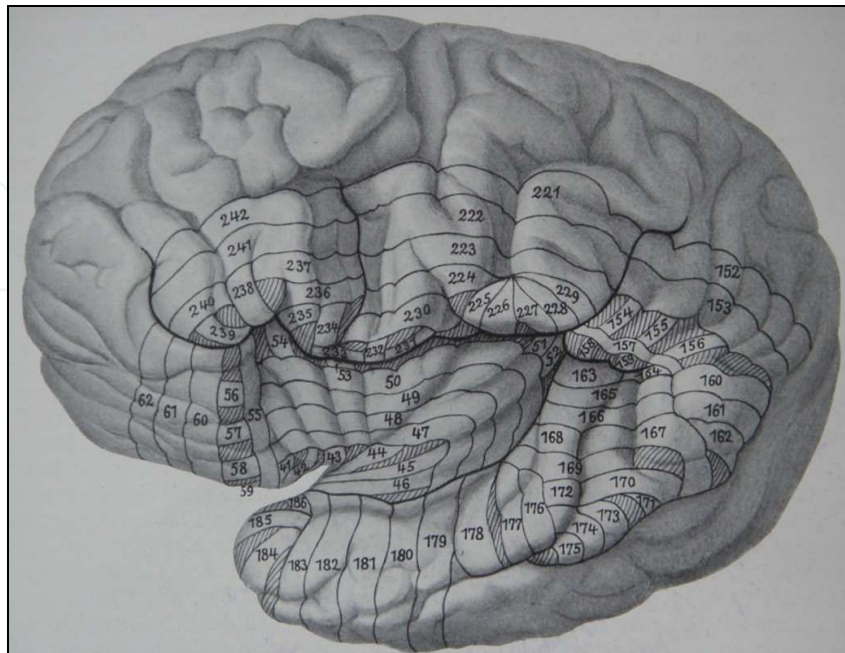


Fig. 6. Indication on the convex cerebral facies around the lateral (Sylvian) fissure of the von Economo & Koskinas (1925, 2008) method for dissecting each hemisphere into an average of 280 4mm-thick blocks perpendicular to the course of each gyrus for cytoarchitectonic study; hatched areas indicate the “cancelled” tissue

Sirs, in the phylogenetic line of living beings, nature, at times acting slowly and at times saltatorily, but always continually, produces new complex and viable animal forms. The same resourceful force that has given over the eons wings to the eagle to fly, has indirectly bestowed humans, by understanding their mind, with the capacity to construct wings themselves in order to defeat the law of gravity and to conquer the air. Nonetheless, the mind has its organic locus, its seat, its altar in the cerebral cortex. That is why one would be justified in saying that the anatomical and the physiological exploration of that noblest of organs deserves the utmost attention of science. The mind which explores and tends to subjugate everything, which tames everything and cannot be tamed, has to fall.”

### 2.3 Response by Spyridon Dontas, annotator

“The work of Drs. Economo and Koskinas is monumental and constitutes a milestone of science, opening up new pathways towards the understanding of the brain from an anatomical, physiological and pathological viewpoint. It further forms the first comprehensive reference on the architecture of the adult human brain. And because the most precise of known methods was used, the optical, and through it a reproduction of the structure of the brain was achieved, in the natural, I reckon that this work will persevere as an everlasting possession of science. I further wish that Drs. Economo and Koskinas continue and complement their work, studying the remaining parts of the nervous system as well, to the great benefit of science.”



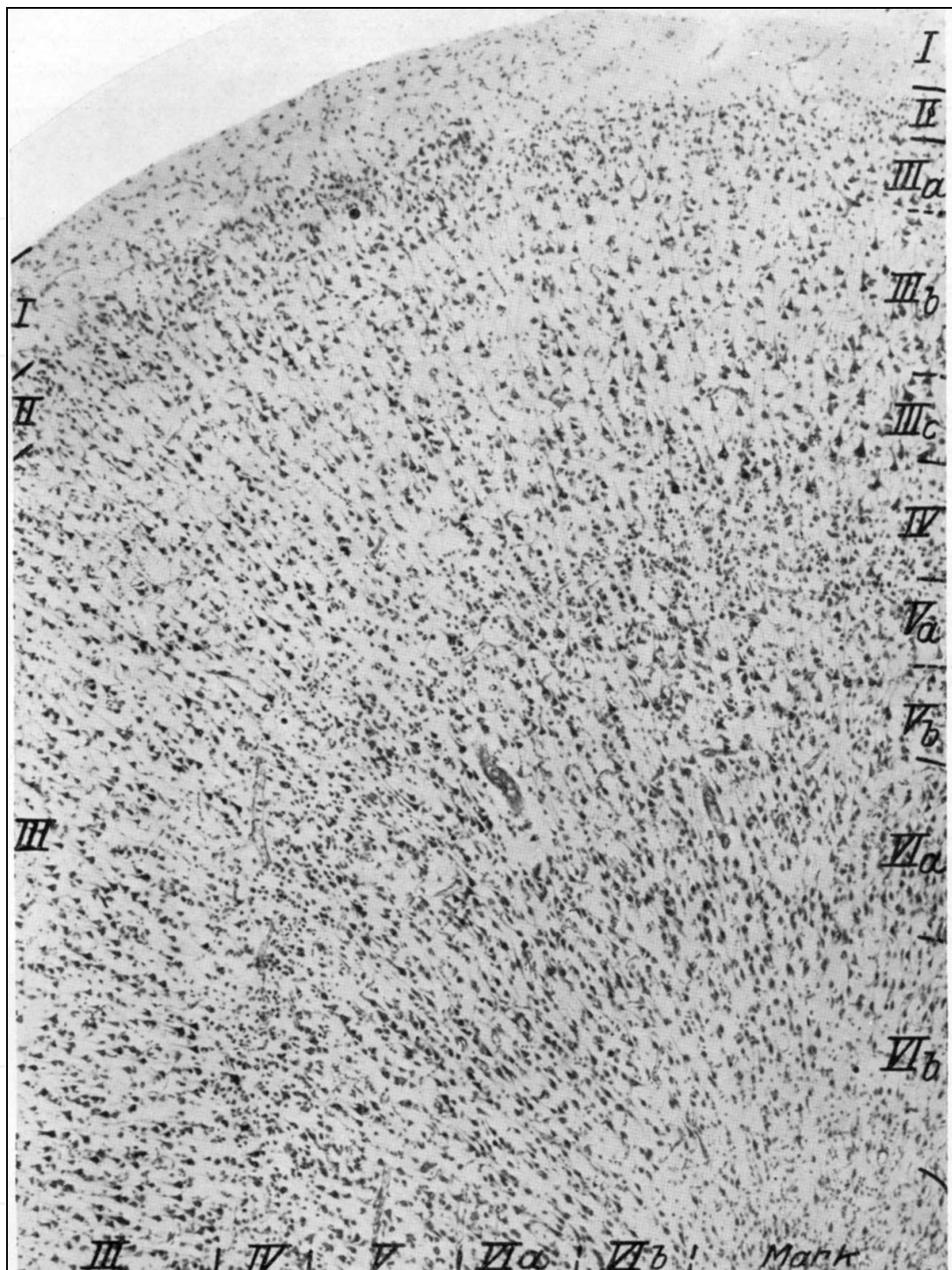


Fig. 7. Section of the dome of a gyrus from the frontal lobe of a human cerebral hemisphere, showing the normal six-layered (hexalaminar) cortex. The white matter (*Mark* in German), which is devoid of nerve cells, is seen on the lower-right hand corner. The six superimposed cortical cell layers are denoted in Latin numbers (I-VI). Photographed with a Carl Zeiss 2.0 cm Planar, a special objective lens with a considerably larger field than could be obtained with common microscopy objectives, especially valuable for large area objects under comparatively large magnifications and an evenly illuminated image free from marginal distortion. Planar micro-lenses are used without an eyepiece.  $\times 50$  (von Economo, 2009)

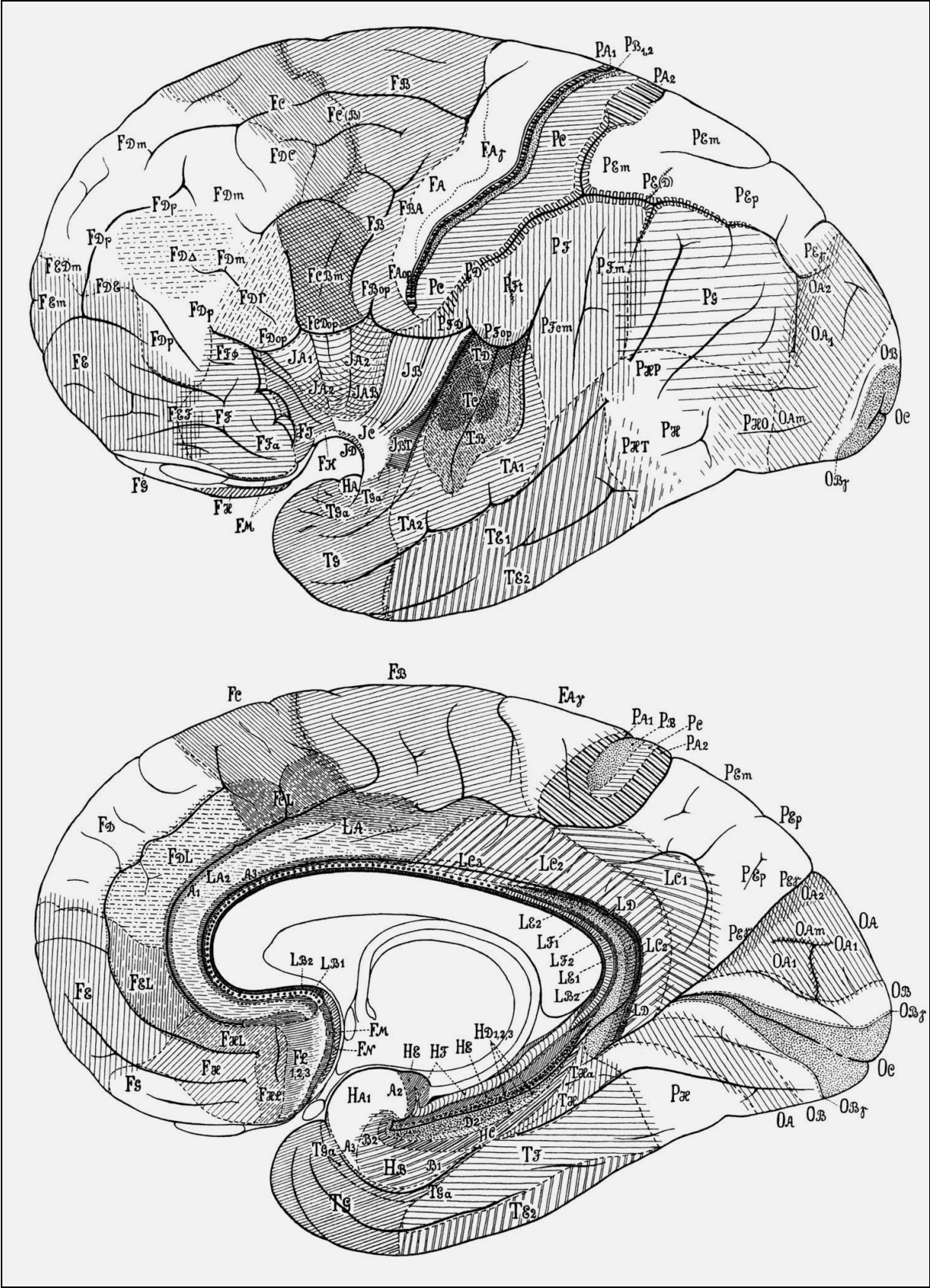
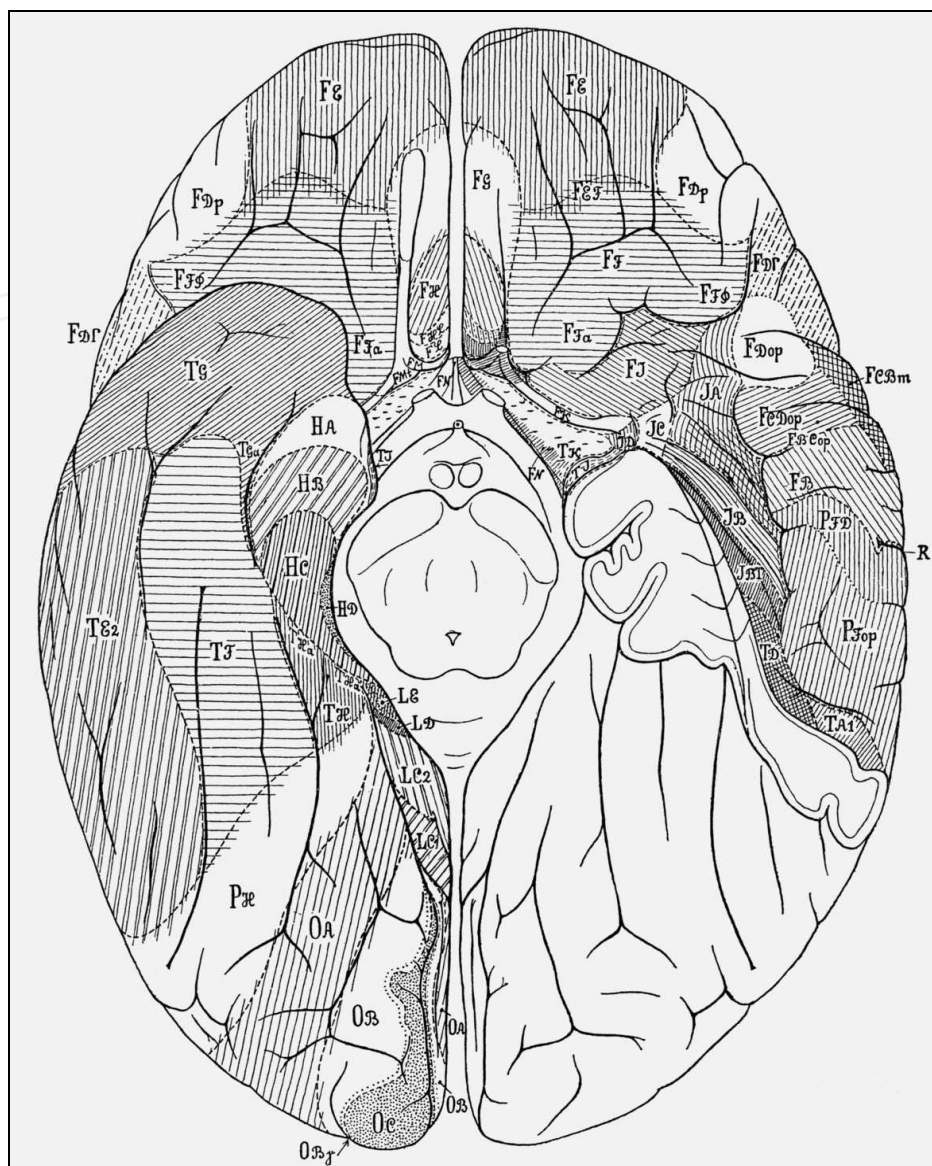


Fig. 8. The cytoarchitectonic map of von Economo and Koskinas, depicting their 107 cortical modification areas on the convex and median hemispheric facies of the human cerebrum









### 3. Conclusion

Besides a histological mapping criterion, variations in cellular structure (cytoarchitecture) of the mammalian cerebral cortex reflect regional functional specificities linked to individual cell properties and intercellular connections. With the current interest in functional brain imaging, maps of the human cerebral cortex based on the classical cytoarchitectonic studies of Korbinian Brodmann (1868–1918) in Berlin are still in wide use (Brodmann, 1909; Garey, 2006; Olry, 2010; Olry & Haines, 2010; Zilles & Amunts, 2010). The Brodmann number system comprises 44 human cortical areas subdivided into 4 postcentral, 2 precentral, 8 frontal, 4 parietal, 3 occipital, 10 temporal, 6 cingulate, 3 retrosplenial, and 4 hippocampal. Following in the footsteps of the Viennese psychiatrist and neuroanatomist Theodor Meynert (1833–1892), who is considered to be the founder of the cytoarchitectonics of the cerebral cortex (Meynert, 1872), von Economo and Koskinas, also working at the University

of Vienna (Triarhou, 2005, 2006), took cytoarchitectonics to a new zenith almost two decades after Brodmann's groundwork by defining 5 "supercategories" of fundamental structural types of cortex (agranular, frontal, parietal, polar, and granulous or *koniocortex*), subdivided into 54 *ground*, 76 *variant* and 107 cytoarchitectonic *modification* areas (von Economo & Koskinas, 1925, 2008), plus more than 60 additional intermediate *transition* areas (von Economo, 2009; von Economo & Horn, 1930).

Topographically, the 107 Economo-Koskinas modification areas are subdivided into 35 frontal, 13 superior limbic, 6 insular, 18 parietal, 7 occipital, 14 temporal, and 14 inferior limbic or hippocampal. Moreover, the frontal lobe is subdivided into prerolandic, anterior (prefrontal), and orbital (orbitomedial) regions; the superior limbic lobe into anterior, posterior and retrosplenial regions; the parietal lobe into postcentral (anterior parietal), superior, inferior and basal regions; and the temporal lobe into supratemporal, proper, fusiform and temporo-polar regions (von Economo, 2009; von Economo & Koskinas, 2008).

The detailed cytoarchitectonic criteria of von Economo & Koskinas (1925, 2008) confer a clear advantage over Brodmann's scheme; their work represents a gigantic intellectual and technical effort (van Bogaert & Théodoridès, 1979), an attempt to bring the existing knowledge into a more orderly pattern (Zülch, 1975), and the only subdivision to be later acknowledged by von Bonin (1950) and by Bailey & von Bonin (1951). It is meaningful that basic and clinical neuroscientists adopt the Economo-Koskinas system of cytoarchitectonic areas over the commonly used Brodmann areas (see also discussion by Smith, 2010a, 2010b). Brodmann (1909; Garey, 2006) described the comparative anatomy and cytoarchitecture of the cerebral cortex in numerous mammalian orders, from the hedgehog – with its unusually large archipallium – up to non-human primate and human brains; he introduced terms such as *homogenetic* and *heterogenetic formations* to denote two different basic cortical patterns, which, respectively, are either derived from the basic six-layer type or do not demonstrate the six-layer stage. Brodmann was intrigued by the phylogenetic increase in the number of cytoarchitectonic cortical areas in primates, and was astute in pointing out the phenomenon of phylogenetic regression as well (Striedter, 2005). Vogt & Vogt (1919) laid the foundations of fiber pathway architecture; they defined the structural features of allocortex, proisocortex, and isocortex, and extensively discussed the differences between paleo-, archi-, and neocortical regions (Vogt & Vogt, 1919; Vogt, 1927; Zilles, 2006).

Combining cyto- and myeloarchitectonics, Sanides (1962, 1964) placed emphasis on the transition regions (*Gradationen*) that accompany the "streams" of neocortical regions coming from paleo- and archicortical sources (Pandya & Sanides, 1973). [Vogt & Vogt (1919) had already spoken of "areal gradations".] The idea of a "koniocortex core" and "prokoniocortex belt areas" in the temporal operculum (Pandya & Sanides, 1973) was modified by Kaas & Hackett (1998, 2000), who speak of histologically and functionally distinct "core", "belt" and "parabelt" subdivisions in the monkey auditory cortex, with specified connections.

There are three major advantages in using the system of cytoarchitectonic areas defined by von Economo and Koskinas as opposed to the maps defined by Brodmann (von Economo, 2009; Triarhou, 2007a, 2007b):

### 3.1 Timing of publication

Brodmann published his monograph in 1909. Von Economo began work on cytoarchitectonics in 1912, with Koskinas joining in 1919; their *Textband* and *Atlas* were published in 1925, almost two decades after Brodmann, and comprised 150 new discoveries

(Koskinas, 1931, 2009), including the description of the large, spindle-shaped bipolar cells in the inferior ganglionic layer (Vb) of the dome of the transverse insular gyrus, currently referred to as “von Economo neurons” (Watson et al., 2006) – although a more accurate term would be “von Economo-Koskinas neurons”. Ngowyang (1932) appears to be the first author to refer to fusiform neurons as “von Economo cells”.

### 3.2 Defined cytoarchitectonic fields

Brodmann defined 44 cortical areas in the human brain. Von Economo and Koskinas defined 107 areas (von Economo, 2009; von Economo & Koskinas, 2008), plus another more than 60 *transition* areas (von Economo, 2009), thus providing a greater “resolution” over the Brodmann areas for the human cerebral hemispheres by a factor of four. Brodmann correlations can be found in the *Atlas* (von Economo & Koskinas, 2008) and in a related review (Triarhou, 2007b).

### 3.3 Extrapolated versus real surface designations

Brodmann maps are commonly used to either designate cytoarchitectonic areas as such, or as a “shorthand system” to designate some region on the cerebral *surface* (DeMyer, 1988). Macroscopic extrapolation of Brodmann projection maps are effected on the atlas of Talairach & Tournoux (1988), rather than being based on real microscopic cytoarchitectonics. Such a specification of Brodmann areas is inappropriate and may lead to erroneous results in delineating specific cortical regions, which may in turn lead to erroneous hypotheses concerning the involvement of particular brain systems in normal and pathological situations (Uylings et al., 2005). On the other hand, the unique sectioning method of von Economo and Koskinas, whereby each gyrus is dissected into blocks *always perpendicular to the gyral surface*, be it dome, wall or sulcus floor, essentially offers a “mechanical” solution to the generalized mapmaker’s problem of flattening nonconvex polyhedral surfaces (Schwartz et al., 1989), one of the commonest problems at the epicentre of cortical research.

Furthermore, microscopically defined borders usually differ from gross anatomical landmarks, cytoarchitectonics reflecting the inner organisation of cortical areas and their morphofunctional correlates (Zilles, 2006). Despite the integration of multifactorial descriptors such as chemoarchitecture, angioarchitecture, neurotransmitter, receptor and gene expression patterns, as well as white matter tracts, it is clear that the knowledge of the classical anatomy remains fundamental (Toga & Thompson, 2007). The structure of cortical layers incorporates, and reflects, the form of their constitutive cells and their functional connections; the underpinnings of neuronal connectivity at the microscopic level are paramount to interpreting any clues afforded by neuroimaging pertinent to cognition.

## 4. Acknowledgment

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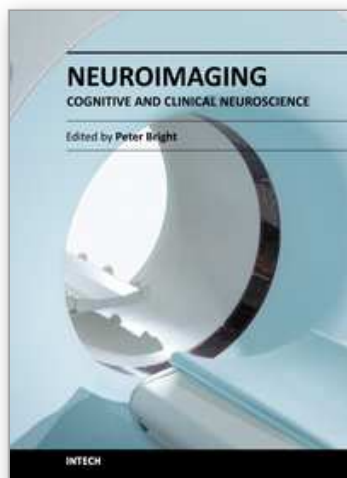
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The rate of technological progress is encouraging increasingly sophisticated lines of enquiry in cognitive neuroscience and shows no sign of slowing down in the foreseeable future. Nevertheless, it is unlikely that even the strongest advocates of the cognitive neuroscience approach would maintain that advances in cognitive theory have kept in step with methods-based developments. There are several candidate reasons for the failure of neuroimaging studies to convincingly resolve many of the most important theoretical debates in the literature. For example, a significant proportion of published functional magnetic resonance imaging (fMRI) studies are not well grounded in cognitive theory, and this represents a step away from the traditional approach in experimental psychology of methodically and systematically building on (or chipping away at) existing theoretical models using tried and tested methods. Unless the experimental study design is set up within a clearly defined theoretical framework, any inferences that are drawn are unlikely to be accepted as anything other than speculative. A second, more fundamental issue is whether neuroimaging data alone can address how cognitive functions operate (far more interesting to the cognitive scientist than establishing the neuroanatomical coordinates of a given function - the where question).

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