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Challenging the supremacy of the frontal lobe: Early views (1906–1909) of Christfried Jakob on the human cerebral cortex

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ABSTRACT

This article focuses on a series of six studies that address functional localization in the frontal lobe; they were published in Argentina between 1906 and 1909 by Christfried Jakob (1866–1956), one of the great thinkers in early 20th century neuropathology and neurophilosophy. At that time, the localization-holism controversy was at a peak, having been triggered by the historic Marie-Déjerine aphasiology debate. Jakob held the view that constitutive physiological elements of cognition are localized. Nonetheless, he cast doubt on phrenological approaches that considered the frontal lobe as ‘superior’ to the other cortical regions. Jakob studied the human frontal lobe from fetal life through senility, in normality and pathology, including tumors, injuries, softening, general paralysis and dementia. Based on those finds, he considered strict localization theories a dead-end. Taking a critical look at Flechsig’s ideas on the parallel ontogenies of frontal association centers and intellect, Jakob argued that the frontal lobe does not carry any selective advantage over the remaining human cerebral lobes or even over the frontal lobe in non-human primates. Regarding lesion experiments in laboratory animals, he pointed to methodological caveats, such as insufficient recovery time, that may lead to disorientating conclusions, and rejected elite brain research, calling it superficial and inexact. Jakob was convinced that the verification of the anatomical connections of the frontal lobe would elucidate its functions. Thus, he viewed the frontal lobe as a central station receiving input via olfactory pathways and thalamic radiations, pertinent to muscular and cutaneous senses, and attributed a perceptive character to a brain region traditionally associated with productive functions. Modern neuroscience seems to support Jakob’s rejection of distinguishable motor and sensory regions and to adopt a cautious stance concerning over-simplified localization views.

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1. Introduction

After more than a century of cortical research, frontal lobe function still poses challenges. The complexity of the cerebral

cortex has led authors to consider it anything from ‘the apparatus of civilization’ to an organ, the removal of which may not always lead to behavioral deficits (Teuber, 2009). The fact that the human frontal cortex occupies one-third of the

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total cortical surface has instilled in researchers the expectation that the unveiling of frontal lobe function might explain the uniqueness of human behavior (Raichle, 2002).

A long debate has been taking place with regard to the functional localization of higher neurocognitive processes in the frontal lobe. Modern theoretical stances fall into a continuum that ranges from fractionated approaches to central concepts; at the same time, attempts are being made to reconcile contrasting views. The common denominator of fractionated approaches (cf. Koechlin et al., 2003; Shallice, 2002; Shallice and Burgess, 1996; Stuss et al., 2002) is the belief that there is no unitary frontal lobe process. The anterior part of the brain rather subserves multiple distinct control processes that underpin executive functions (Godefroy et al., 1999). Within such a framework, modularity and fractionation may even pertain to higher human abilities (Baddeley, 1996; Stuss et al., 2002). A more central concept has been put forth by Duncan and Miller (2002), who reject a fixed functional specialization and highlight the adaptability of select regions of the prefrontal cortex in order to complete a goal-directed activity. Finally, Stuss (2006) argues that the debate between fractionation and adaptability is a false debate and suggests that brain networks may be both locally segregated and functionally integrated (Yeterian et al., 2012, *this issue*; Catani et al., *in press*). Marshaled evidence showing the recruitment of the same frontal regions for different cognitive demands (Duncan and Owen, 2000) suggests that in spite of the fractionation, frontal processes are applicable to many domain-specific modules, and therefore are domain-general (Stuss, 2006).

However, the issue of functional localization has been at the core of neuropsychological research, as well as of philosophical delving, since the 19th century (Catani and Stuss, 2012, *this issue*). Although the idea of specific cerebral localizations of physiological functions was adopted before 1861 by several researchers including Gall and Bouillaud (cf. Finger, 2000), it was Broca's (1861) lecture to the Paris Anthropological Society that brought it forcefully to the scientific world (Lorch, 2008). The second of the two liveliest debates in the history of aphasiology took place when Marie questioned Broca's views, while Déjerine defended localization at a special joint meeting of the New York and the Philadelphia Neurological Societies and at the Neurological Society in Paris two years later, triggering a debate that spread internationally (cf. Tsapkini et al., 2008). At the same time, Jakob (1866–1956), a neurobiologist working in Buenos Aires, would adopt an integrative approach in his attempt to elucidate cortical function.

Born and educated in Germany, Jakob (Fig. 1) went to Argentina in July 1899. At that time, he had already made an international name for himself through his early brain Atlas (Figs. 2 and 3). Zülch (1975) credits Jakob (1899, 1901, Plate 15.5) for demonstrating that, at the direct corticospinal level, the pyramidal pathway is not yet myelinated in the newborn human; as Flechsig (1927) had described, only pathways that pass from motor cortex to the midbrain are myelinated at birth. In all, Jakob left 30 books and 250 articles that cover developmental, evolutionary, anatomical, pathological and philosophical issues in neurobiology (Barutta et al., 2011; Moyano, 1957; Triarhou and del Cerro, 2006a, 2006b; 2007).



Fig. 1 – A sketch of Christfried Jakob by his student and biographer López Pasquali (1965). Signature from Orlando (1966).

The frontal lobe occupied Jakob's thought constantly in a path of enquiry spanning over five decades. Having studied the frontal lobe in its various developmental stages, and in neuropathological conditions, Jakob (1906a, 1907c) cast doubt on its 'supremacy' (Fig. 4). He pointed to potential historical reasons—linked to classical Greek philosophy—that might explain the importance attached to it. Jakob noted that physical characteristics, such as the upright posture, the extremities, and the extended forehead, distinguish humans from animals. In particular, Jakob (1943) considered the 'Olympian forehead', artistically expressed in the sculptures of Zeus, as the symbol of 'humanization'.

Jakob's contributions, written in German and Spanish, have been largely neglected in the English scientific literature. The present study aims at highlighting key concepts from his 'early' period. In that context, we provide selected translated passages from six papers, published between 1906 and 1909 (Jakob, 1906a, 1906b, 1906c, 1907a, 1907b, 1909), that address biological, anatomo-clinical and pathophysiological aspects of the frontal lobe. A psychobiological theory on the gnoses and praxes that culminated during Jakob's 'middle' period is presented elsewhere (Théodoridou and Triarhou, 2010).

2. Neuroanatomical studies

Jakob constantly viewed morphology in a functional context (Tsapkini et al., 2008). He believed that the elucidation of the

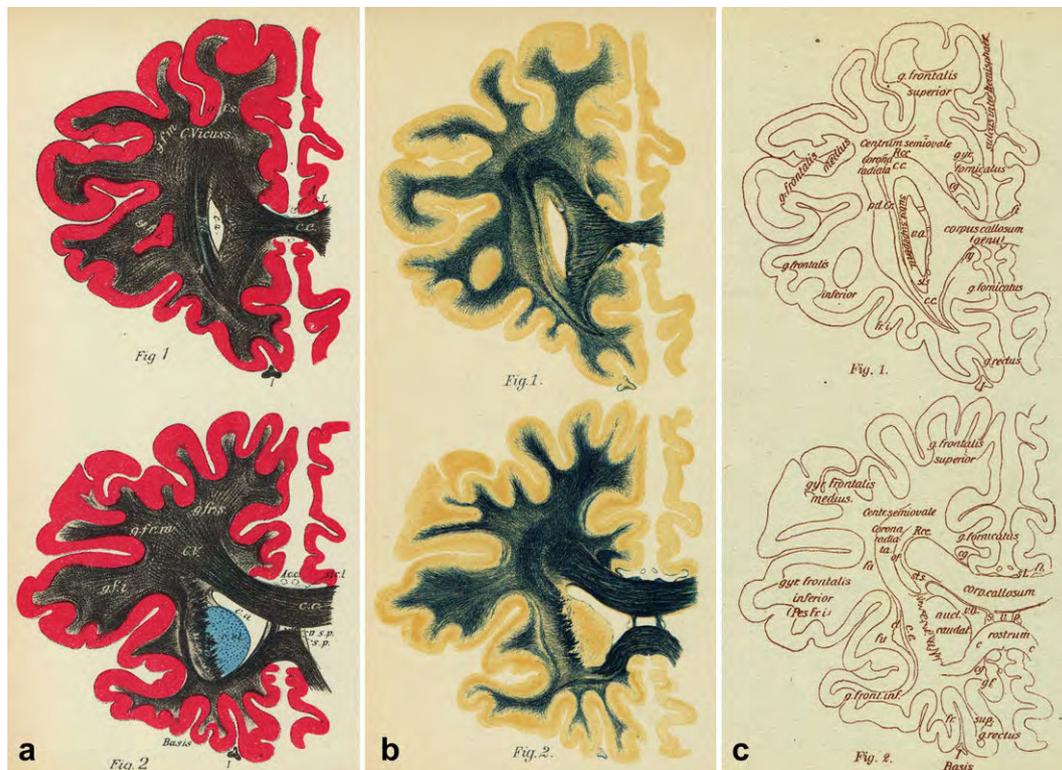


Fig. 2 – Drawings of coronal sections of the frontal lobe by Jakob for his early brain Atlases. (a) Plate 24 from the first edition (Jakob, 1895, 1896): frontal sections through the knee of the corpus callosum and the anterior segment of the frontal lobes (upper) and through the head of the caudate (lower). Abbreviations: *g.f.s.*, superior frontal gyrus; *g.f.m.*, middle frontal gyrus; *g.f.i.*, inferior frontal gyrus; *c.a.*, anterior horn of lateral ventricle; *f.a.*, lateral association bundles; *C.Vieuss.*, centrum semiovale; *I*, olfactory bulb; *s.p.*, septum pellucidum; *c.st.*, head of the caudate nucleus; *c.i.*, anterior limb of the internal capsule. (b, c) Plate 28 from the second edition and explanatory diagram (Jakob, 1899, 1901). Abbreviations: *Rcc.*, radiation of corpus callosum; *pd.Cr.*, base of corona radiata; *ft*, tangential fibers; *st.s.*, central gray matter of the ventricle; *v*, ventricle; *of*, occipitofrontal fasciculus; *cg*, cingulum; *fa*, arcuate fasciculus; *fu*, uncinuate fasciculus; *ce*, external capsule; *cl*, claustrum; *pes fr.i.*, foot of inferior frontal gyrus; *sL*, nerves of Lancisi; *st.a.*, central gray matter.

anatomical connectivity of the frontal lobe would decipher its functions. Therefore, the anatomo-clinical approach was taken as the safest way in reaching conclusions on function. Jakob emphasized the importance of studying connections, an idea consistent with the current hodological trend (cf. Catani and ffytche, 2005; ffytche and Catani, 2005; Thiebaut de Schotten et al., 2012, this issue). Furthermore, his writings on connections seem attuned to more recent theories of frontal systems and neural networks, such as Alexander et al.'s (1986) influential concept of parallel but segregated frontal-subcortical circuits that has been put into a clinical framework. An in-depth discussion of the association between frontal-subcortical circuits and neurobehavioral disorders can be found in Chow and Cummings (1999) and other papers of the special issue (Krause et al., 2012, this issue; Cubillo in press, 2012; Langen et al., in press).

In studying the structure of the frontal lobe, Jakob did not see any substantial differences from the remaining lobes of the cerebral hemispheres: "The frontal lobe has three categories of fibers just like the other lobes: afferent and efferent projection fibers, association fibers and commissural fibers... Through the study of the afferent pathways we understand that in the major part of the frontal lobe, covering the whole of

its convexity lies the great center of the muscular senses of a higher order" (Jakob, 1906b).

Concerning the connections between the frontal gyri and the Rolandic motor areas via 'U' fibers, Jakob (1906b) wrote: "These fibers join the superior frontal gyrus with motor foci that innervate the lower extremities, relate the middle frontal gyrus with the foci of the arms, and the inferior frontal gyrus with facial-lingual movements... Moreover, there exist short association fibers that connect the three gyri among them, and commissural fibers that, passing through the corpus callosum, enable the communication between the frontal gyri of the two sides... Thus, we come across the existence of an apparatus inserted between the muscles of the periphery and the cerebellum on one side and the Rolandic centers on the other" (Fig. 5).

Jakob (1906c) described the sensory-muscular pathways that arrive at the frontal lobe via the cerebellum, the red nucleus and the thalamus, concluding: "Although it is doubtful whether tactile senses arrive at the frontal lobe, it is true that numerous muscular sensory inputs enter the frontal lobe." In concordance with such an argument, Cappe et al. (2009) demonstrated the existence of thalamic projections to the cerebral cortex using neuroanatomical track-tracing

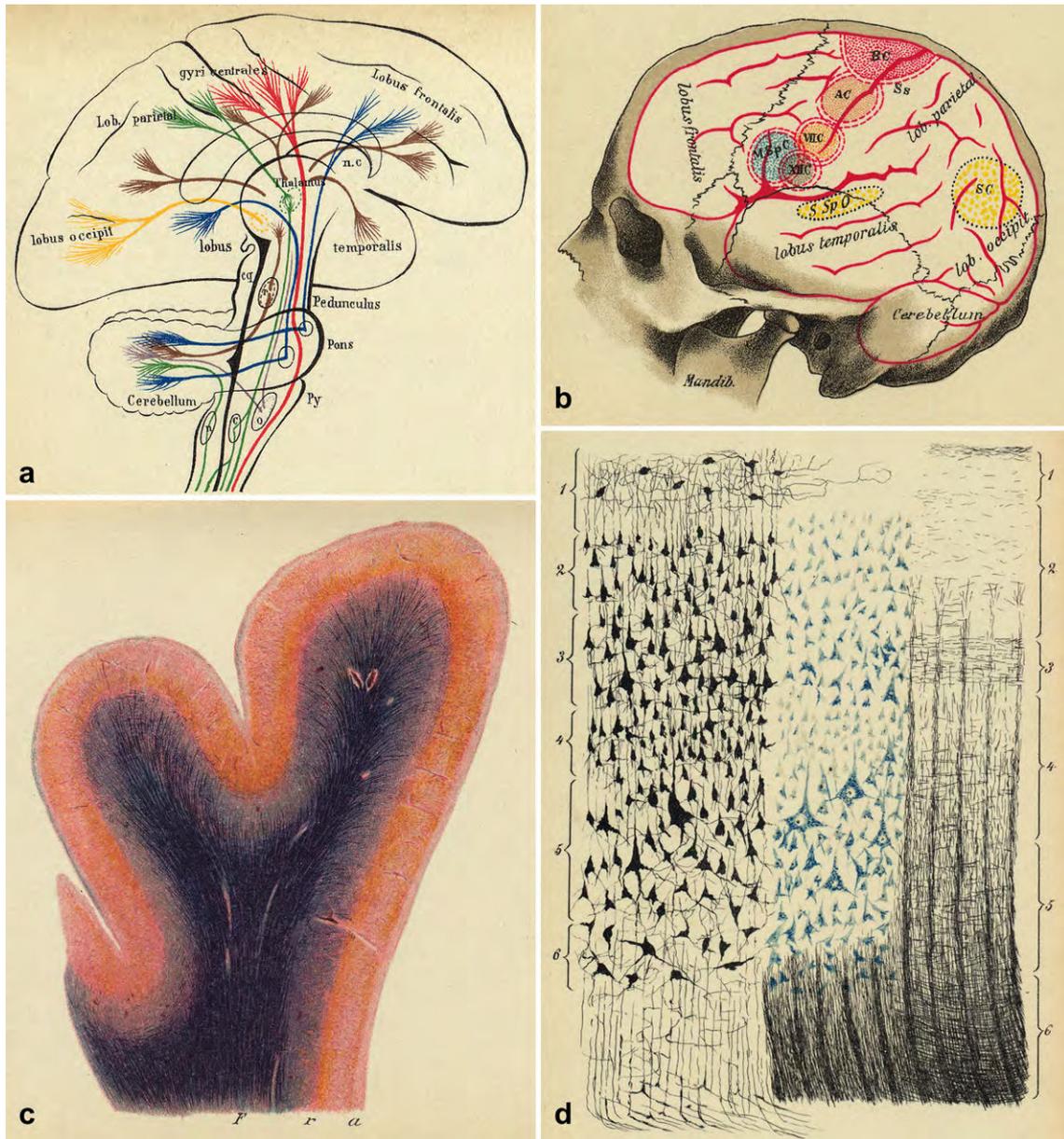


Fig. 3 – Additional drawings by Jakob from the second edition of his early brain Atlas (Jakob, 1899, 1901). (a) Plate 56.1 showing a general view of projection paths. Fibers forming the corona radiata enter the optic thalamus (brown). The frontal and temporal pontine pathway reaches the cerebellum through the contralateral middle cerebellar peduncle (blue). The pyramidal tract appears red, the sensory tract green, the cerebello-olivary tract violet, the optic radiation yellow, and the brachia brown. (b) Plate 21.3 depicting the position of psychomotor and psychosensory cortical centers in the cavity of the skull. Abbreviations: BC, motor center for lower extremities; AC, motor center for upper extremities; VIIC, XIIC, centers for muscles innervated by the facial and hypoglossal nerves; MSpC, SSpO, motor and sensory speech centers; SC, visual center. (c) Plate 20.1 showing a section from the center of the anterior central gyrus (carmin myelin sheath stain). White matter (F) appears blue-black; radial bundles (r) radiate in all directions and end in the cortex; a, outermost subpial layer. (d) Plate 19 showing the arrangement of cells (left and middle, stained with silver and methylene blue, respectively) and fibers (right) in the cerebral cortex. Cytoarchitectonic layer nomenclature: (1) Stratum zonale; (2) first layer of small pyramidal cells; (3) layer of medium-sized and large pyramidal cells; (4) second layer of small closely packed pyramidal cells; (5) second layer of medium-sized and large pyramidal cells with a few giant pyramidal cells; (6) layer of polymorphous cells. Myeloarchitectonic layer nomenclature: (1) stratum zonale with superficial layer of tangential fibers; (2) superradial reticulum and Bekhterev-Kaes stripe; (3) coarser tangential fibers (stripes of Baillarger, Gennari, Vicq d'Azyr); (4) interradian reticulum of tangential fibers; (5) closely packed radial bundles; (6) medullary layer with radiating white fibers (projection, commissural, and long association tracts) and transverse short association bundles (arcuate fibers of Meynert). For the most part, nerve fibers pass from the cerebral white matter into the cortex; collected in bundles, they enter the second layer of cells, where their terminal fibrils end. These radial bundles (radii) therefore have a vertical arrangement. They are crossed at right angles by other fibers running parallel with the cortical surface and forming the plexus of tangential fibers – the superradial reticulum above the radii, and the interradian reticulum with the radii.

(1933) **La légende des Lobes Frontaux en tant que Centres supérieurs du Psychisme de l'Homme**, par CRISTOFREDO JAKOB (de Buenos-Aires). *Archivos de Psiquiatria y Criminología*, Buenos-Ayres, an V, p. 679-698, novembre-décembre 1906.

L'auteur donne plusieurs observations de lésions des lobes frontaux sans déficit psychique d'aucune sorte. La conclusion de son travail est que les lobes frontaux n'exercent aucune hégémonie sur le reste du cerveau; ce qui est perdu de la personnalité psychique à la suite des lésions étendues des lobes frontaux n'est qualitativement, ni quantitativement différent de ce qui est perdu à la suite de la destruction étendue de tout autre lobe cérébral. F. DELENI.

Fig. 4 – Jakob's 1906 paper abstracted in French in the prestigious *Revue Neurologique* (Jakob, 1907c). The summary reiterates Jakob's conclusion, based on observations that lesions in the frontal lobes do not lead to any substantial mental deficit: "The frontal lobes do not exert any hegemony over the rest of the brain. Any mental deterioration after damage to the frontal lobe does not differ qualitatively or quantitatively from that seen after damage to any other cerebral lobe".

markers. Furthermore, Goldman-Rakic and Porrino (1985) showed that the prefrontal cortex is defined by multiple specific relationships with the thalamus. Performing retrograde tracing experiments, Mitchell and Cauller (2001) examined the corticocortical and thalamocortical afferents to layer I of the rat frontal cortex and affirmed the existence of afferent projections from thalamic nuclei to the frontal lobe.

Based on his anatomical observations, Jakob (1906c) viewed the major part of the frontal lobe as a central station with multiplier and combinatorial characteristics, constantly receiving stimuli from all the motility organs via multiple pathways (Fig. 6). According to Jakob (1911), the various centripetal pathways course into all sectors; thus, the cortex has a perceptive activity over its entire extent (Triarhou, 2010). Jakob's position is compatible with modern views on the function of the anterior parts of the human brain: the prefrontal cortex is considered a locus of synthesis of the outputs of various brain systems which provides the basis for the orchestration of complex behavior (Duncan & Miller, 2002). Furthermore, the role of the frontal lobe in integrating

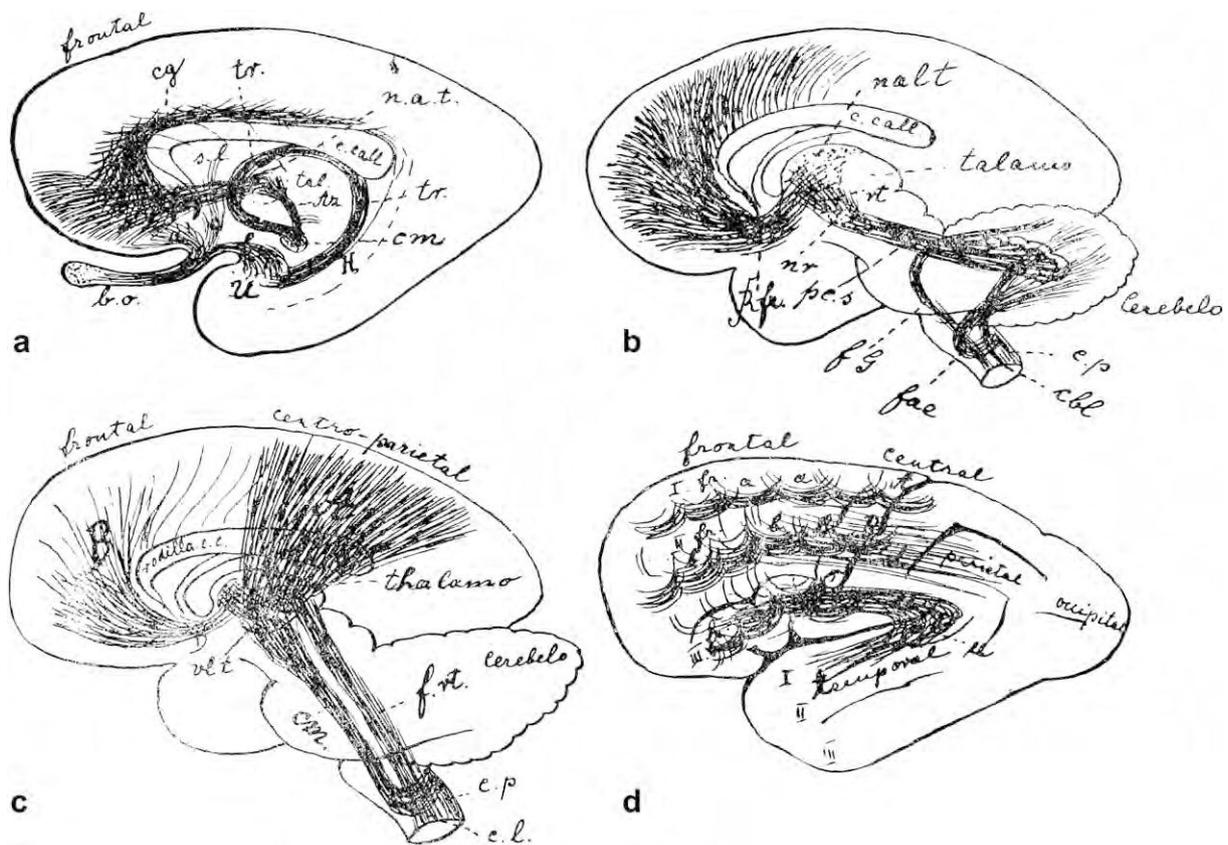


Fig. 5 – Schematic drawings by Jakob (1906b) showing: (a) Olfactory pathways in the frontal lobe. Abbreviations: b.o., olfactory bulb; a, internal root; b, lateral root; sl, septum pellucidum; u, uncus; h, hippocampus; tr, trigonum; cm, mamillary body; Az, bundle of Vicq d'Azyr; nat, anterior nucleus of thalamus; Rf, thalamo-frontal radiation; cg, cingulum. (b) Cerebello-frontal pathways. Abbreviations: cp, posterior spinal fasciculus; cbl, lateral cerebellar bundle; fg, bundle of Gowers; pcs, superior cerebellar peduncle; nr, red nucleus; rt, rubro-thalamic pathway; nalt, anterior lateral thalamic nucleus; Rfr frontal radiations. (c) Direct medullo-thalamo-frontal pathways. Abbreviations: cp, posterior spinal bundle; cl, lateral bundle; f.rt, reticular formation; cm, median band of Reil; vlt, ventral nuclei of thalamus; A, thalamo-Rolandic pathway; B, thalamo-frontal pathway. (d) Association pathways in the frontal lobe. Abbreviations: A, Rolandic center of crus; a, U-fibers of superior frontal gyrus (I); B, brachial center; b, U-fibers of middle frontal gyrus (II); C, facio-lingual center; c, U-fibers of inferior frontal gyrus (III); u, uncinate fasciculus; d, superior longitudinal fasciculus.

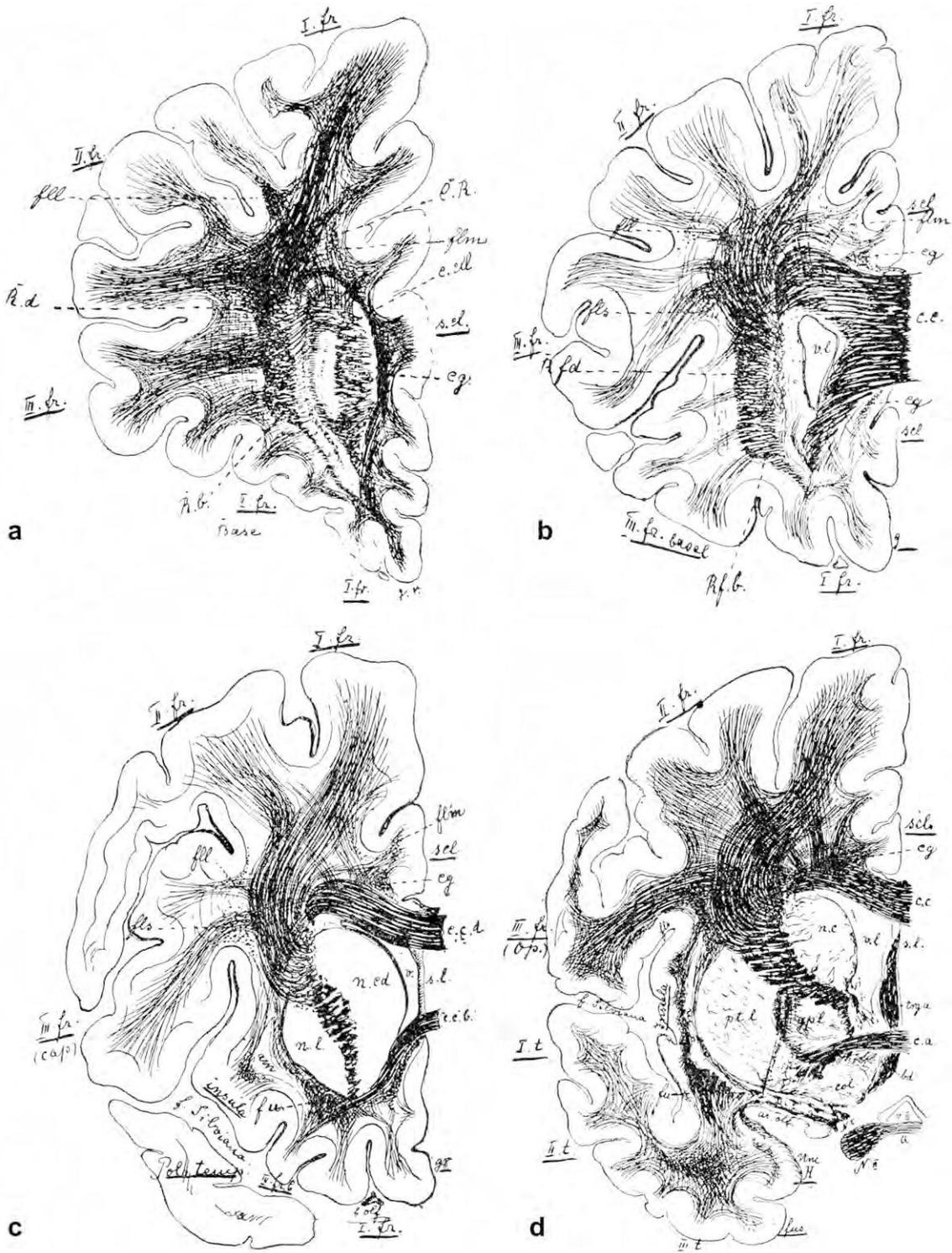


Fig. 6 – Schematic drawings by Jakob (1906c) based on a complete series of serial sections through the frontal lobe; Weigert method to depict fiber pathways. (a) Frontal section (no. 1154) in front of the corpus callosum. (b) Long projection, commissural and association pathways; section (no. 1076) through the knee of the corpus callosum. (c) Projection and commissural pathways and the formation of the internal capsule (frontal radiation); section (no. 948) through the corpus striatum. (d) Section (no. 882) through the posterior region of the frontal lobe with all its long frontal pathways. Abbreviations: fr, frontal; t, temporal; v, ventricle; l, lateral; nc, caudate nucleus; ptl, putamen-lenticular nucleus; gpl, globus pallidus; CR, corona radiata; RD, dorsal radiation of internal capsule; Rb, basal radiation of internal capsule; gr, rectal gyrus; cg, cingulum; flm, fl, fls, medial, lateral and superior longitudinal fasciculus; fu, uncinata fasciculus; cc, corpus callosum; sl, septum pellucidum; am, claustrum; scl, supracallosal gyrus; nl, lenticular nucleus; ca, anterior commissure; v_{III} , third ventricle; NI, olfactory nerve; NII, optic nerve; ar.olf, olfactory area; trga, anterior pillars of trigonum; col, coliculi of corpus striatum.

information from multiple brain areas supports its crucial involvement in learning, comprehension and reasoning (Baddeley, 2002). Frontal and prefrontal regions have been linked to visual, auditory and somatosensory inputs (Fogassi et al., 1996; Graziano et al., 1994, 1999; Wallace et al., 1992). Sensory, mnemonic and response signals that a single neuron displays provide strong evidence that prefrontal neurons behave as sensorimotor integrators (Goldman-Rakic, 2000). Prefrontal cortical neurons are considered to be a part of integrative neural systems that subservise cross-modal interactions across time (Fuster et al., 2000). According to Fuster's (2006) theorizing, actions related to human behavior, reasoning, and language are organized by means of interactions between prefrontal and posterior networks at the top of the 'perception–action cycle.' In non-human primates, multisensory integration takes place in frontal, parietal and temporal areas (Avillac et al., 2005). Thus, mounting evidence shows that much if not all of the neocortex is involved in multisensory integration (Ghazanfar and Schroeder, 2006).

3. Histological studies

3.1. Cytoarchitectonics

Based on the argument that structural differences signal functional specialization, Jakob studied human brain cytoarchitecture (Fig. 3d). Jakob (1906c) summed up his research as follows: "The frontal cortex is organized in the same cell layers, in the same associations of pyramidal cells that are differentiated only by their size, as we notice in the parietal and temporal lobe as well. The only thing that distinguishes the frontal cortex is the restricted variation of the size of the pyramidal cells due to the lack of large and giant pyramidal cells. My studies allow me to admit that toward the feet of the frontal gyri appear the large pyramidal cells covering the background of the precentral sulcus. Moreover, I managed to prove that the frontal cortex contains more cells per square millimeter compared with the Rolandic and the temporal regions. I could not deduce from this fact that the absolute number of cells would be greater in the frontal region compared to the Rolandic or the temporal regions, because the latter have a very high density".

At about the same time, Campbell (1905), a pioneer of cortical cytoarchitectonic parcellation, compiled clinical, anatomical and physiological evidence as a guide to function (ffytche and Catani, 2005). However, it was Brodmann's (1909) opus magnum that changed the view of histological localization in the human cerebral cortex once and for all (cf. Garey, 2006). Brodmann (1913) also produced a subsequent study concentrating on the frontal cortex (Elston and Garey, 2004).

3.2. Myeloarchitectonics

Having studied preparations with the Weigert method (Fig. 6), Jakob (1906c) argued: "As far as frontal myeloarchitectonics is concerned I notice the same disposition of radiating fibers as in other regions... The so-called association layers are identical to the ones of the other lobes and the tangential layer is well developed. On the contrary, the supraradial layer stands out in showing remarkably fewer myelinated fibers... I am inclined to

see a structural inferiority, an idea that is reinforced by the following facts: a diminished total density and density of the various layers, a smaller average cell volume and a less developed supraradial layer." Regarding Flechsig's proposal of a parallel development of myelination pathways and intellect, Jakob wrote: "While the central tracts of the frontal lobe are not completed until several months after birth, Flechsig demonstrated that other regions of the brain develop in a similar fashion, for instance parts of the parietal and temporal lobes, the insula, and the so-called associative centers... Any chronological difference is not of much importance since a child has his frontal center perfectly myelinated before reaching six months of age. However, a newborn infant and one of six months are not easily differentiated with respect to their cognitive development" (Jakob, 1906a).

Myelination in humans continues well into the second decade of life (Yakovlev and Lecours, 1967). Structural magnetic imaging studies have shown gray matter changes in the frontal lobe from adolescence to adulthood (Sowell et al., 1999). In support of Flechsig's claim, the myelination of the frontal lobe has been repeatedly correlated with the development of higher cognitive functions, such as working memory (Nagy et al., 2004) and language (Pujol et al., 2006), while incomplete myelination has been blamed as the underpinning of weak decision-making skills in adults (Giedd, 2004).

Campbell's cytoarchitectonic data led to conclusions close to those of Jakob: "The structural development of the prefrontal cortex is exceedingly low. It presents an extreme of fibre poverty; all its fibre elements are of delicate calibre, and its association system is particularly deficient. Its cell representation is on a similar scale. The cortex is also shallow" (Campbell, 1905).

4. Pathophysiological studies

For the most part of the 19th century, the literature emphasized the role of the frontal lobe based on cases of damage that resulted in profound personality changes. Having studied human brains with frontal lobe tumors, injuries and degeneration, Jakob (1909) pointed to the rareness of 'pure cases'; he highlighted the characteristics that may render pathological specimens inappropriate for drawing secure conclusions. He emphasized that (a) the appearance of symptoms does not necessarily coincide with the onset of the disease; thus, progression may be difficult to determine; (b) tumors compress the brain parenchyma; (c) lesions of vascular origin lead to widespread degeneration; and (d) brain damage may cause inflammation or concussion which may affect the whole brain (Jakob, 1906c, 1909).

von Monakow (1904, 1910) underlined certain factors that had been overlooked by other investigators who studied lesions, i.e., the effects of inflammation, the lack of aseptic conditions during surgery, and the distant effects of local damage over time (Finger, 1994). Further caution has been expressed by Teuber (2009) about the contradictions found in the clinical literature: case studies may involve either massive lesions extending beyond the frontal lobe or small, unilateral, or asymmetric lesions with correspondingly small and easily compensated effects.

5. Comparative studies

Jakob's phylogenetic studies, from the human brain to over 100 species of the Patagonian fauna (Jakob, 1912a, 1912b; Jakob and Onelli, 1913, Triarhou, 2010), provided him with the bases for formulating the following ideas:

“The development of the frontal lobes increases from lower to higher mammals in a continuous and constant relation, whereas in other vertebrates there are no hemispheres with a cortex comparable to those of mammals. It is obvious that the region located in front of the cruciate sulcus (a structure homologous to the central sulcus) increases in size and in the number of gyri it possesses from the marsupial to the rodent, from the rabbit to the dog, from the dog to the monkey, and approaches the size and complexity of humans only in anthropomorphous apes...¹ Although the external morphology progresses from lower to higher scale in a constant manner, the same process does not occur in the internal structure... We see, then, that what is true about the process of comparative development in the frontal lobe is true in all the other lobes as well. Perhaps there are greater variations in one structure than another; but such variations are slight and it would be a highly difficult, if not impossible, venture to find a fundamental exception for the frontal lobe” (Jakob, 1906a).

Elsewhere, he wrote: “When the frontal lobes of the different mammals, of ape and man are compared, the concord of the fine cortical structure strikes our attention; it is hard to encounter well defined differences... I myself noticed that the radiating fibers of the frontal lobe in apes are of a smaller calibre in comparison to other regions, a fact that has already been mentioned for humans. As far as the pyramidal cells are concerned ape shows all the different human types... What distinguishes the human frontal lobe is only the number of large and giant pyramidal cells... If the frontal lobe were such a superior center that it would differentiate by its functions humans from animals, then we should have met more evident differences in histological structure. According to my studies, I am inclined to believe that the similarities between the frontal cortical regions of some higher animals (for example apes) and humans are greater than the differences. This fact comes to demonstrate that the problem of the superior human functions does not lie in their localization in this or that lobe, but in factors of another nature” (Jakob, 1906c).

From the beginning of the 20th century, the extraordinary human cognitive development has been attributed to the large size of the frontal lobes. Cytoarchitectonic studies show a very similar organization between human and macaque monkey prefrontal cortex (Petrides, 2005; Petrides et al., 2012, this issue). Magnetic resonance imaging studies (Semendeferi et al., 2002) show that the frontal cortex of humans and great apes occupies a similar proportion of the cortex of the cerebral hemispheres. Accordingly, the enlargement of the human brain has generally preserved the relationship

between its major lobes (Risberg, 2006). A relative increase of association cortex due to encephalization cannot lead to a regional expansion of the frontal association areas since all four cerebral lobes have both primary and association cortices; therefore, such an expansion should be common to all (Allen, 2009). For further discussion see also Petrides et al., (2012, this issue), Yeterian et al., (2012, this issue) and Thiebaut de Schotten et al., (2012, this issue).

6. Experimental animal studies

Laboratories where experiments on animals were conducted have been one of the most vivid battlefields in the localizationist–antilocalizationist controversy. The experimental confirmation of motor cortex in dog brain by Fritsch and Hitzig (1870) was a landmark in the history of functional localization (Catani and Stuss, 2012, this issue). This tradition continued with new mosaicists and holists. Jakob (1906b) points out: “Goltz, Ferrier, Hitzig and Bianchi observed that animals that had both frontal lobes removed present remarkable alterations in intellect and character, such that they become irritable and have an increased tendency to bite... These experimenters did not sufficiently prolong their observations, and neither were they able to exclude as an explanation the consecutive inflammation or infections caused by the operation. New experimental verification, performed with meticulous care by Munk, Grossglik, Horsley and Schafer (1888), did not absolutely verify any of the previous observations. They found that once the animals had passed the first moments of postoperative excitation, they all returned to their status quo”.

The vulnerability of the first series of experiments was also highlighted by Jacobsen et al. (1936), who attributed it to (a) the lack of objective measures of the degree and nature of behavioral deficits and (b) the lack of the demonstration that lesions of equal extent in other cortical regions do not cause dementia of the same severity.

7. Frontal lobe and higher cortical functions

According to Jakob's model, intelligence, memory and the like are needed for handling abstract concepts (Jakob, 1906c). Similarly, the view that psychical terms do not have localizable physiological correlates was expressed by Jackson and embraced by Freud, Goldstein, Pick, and Head (Meyer, 1974).

In 1906 Jakob wrote: “Consciousness is formed gradually as a result of the chaining of different cortical operations. It is impossible to view it as a localizable, special power separate from such processes. Consciousness is the manifestation of the synchronization of its components, since it is afflicted whenever any one of such components is afflicted. Intelligence is a quality par excellence that represents the rapid and safe function of the sensory, motor and associative apparatus. It cannot be localized, because it is a phenomenon inseparable from the overall cerebral process. Character is a mode of motor reactions congenitally imprinted on cortical elements. It intervenes in the transformation of the sensory and the motor functions and it is manifested in every action. Character is a quality, not a substantial power; therefore it could

¹ This was not a new observation: it is found, for instance, in the anatomy of Owen (1866–1868).

not be localizable. With the word ‘memory’ we designate an essential function that touches upon all the biological processes in the wider sense and especially upon the cortical processes. Will is the result of the inhibitory or productive influence that is exerted by gradually acquired associations on the inferior reflex actions via the motor centers. It has its origin in the association centers that cover the entire cortex. Only a determined voluntary act may be limited in a specific portion of the grand apparatus; nevertheless, for the production of such an act all the hemispheric regions intervene with greater or lesser intensity” (Jakob, 1906c).

Jakob’s neurophilosophical writings became gradually refined and expanded in the course of his career. Well before neurophilosophy emerged as a formal scientific discipline, Jakob had written at least 14 philosophical works (López Pasquali, 1965), touching upon issues such as the relation between biogenesis and philosophy (Jakob, 1914) and the philosophical meaning of the human brain (Jakob, 1945; Théodoridou and Triarhou, 2010). Today, theories seek to elucidate the neural correlates of consciousness (cf. Crick & Koch, 1990). The so-called ‘hard problem’ lies in the consideration of consciousness as an ‘emergent’ property ‘arising’ from functional elements of the neurocognitive structure without attributing a dualistic character to it (Kouider, 2009). For example, according to Edelman and Tononi’s model of a constantly shifting dynamic core (cf. Edelman, 1992; Tononi and Edelman, 1998), consciousness arises from the fast integration within a dynamic core of interacting elements. Other neurobiological theories, such as the global neuronal workspace (Dehaene et al., 1998; Dehaene and Naccache, 2001) highlight the interconnection between multiple cerebral modules that enables the broadcasting of information (Kouider, 2009). Whereas “proving the case for synchronization in the human brain” is still considered technically demanding (Zeman, 2001), Jakob conceived, in an impressive manner, the idea of synchronization of neuronal activity as the underlying mechanism of consciousness, more than a hundred years ago. Jakob’s interpretation is consistent with the view that consciousness is to be correlated with a non-continuous event determined by synchronous activity in the thalamocortical system (Ribary et al., 1994). The transient synchronization of brain operations is considered to have the potential to construct unified and relatively stable neural states that underlie conscious states (Fingelkurts et al., 2005). The perception of volition seems to be generated in specific networks with the parallel activation of the global neuronal workspace (Hallett, 2007). The role of inheritance in behavior has been shown by selection and strain studies for animal behavior and by twin and adoption studies for human behavior (Plomin, 1990). Further evidence for the endogenous nature of traits derives from studies of behavior genetics, parent-child relations, personality structure, animal personality, and the longitudinal stability of individual differences (McCrae et al., 2000).

To conclude, Jakob tackled the ‘terra incognita’ of cognition with a multi-level approach in order to avoid bias. He was critical of oversimplifying localization explanations. Further, Jakob understood that it is essential to realize the limitations and misdirections involved in any attempt to decipher the brain–mind relationship. Being aware of such limitations, he searched for diverse clues, and largely relied on the anatomo-

clinical approach. His concrete knowledge of neuroanatomy, coupled with his ingenuity, enabled him to produce knowledge that can be corroborated today via sophisticated tracing techniques. In a broad framework, studying Jakob’s papers helps to correct and reconstruct an important episode in neurological history. Moreover, new English translations of such works will make them accessible by a wider audience. Given that the riddle of the human frontal lobe remains a central issue in modern neurobiology, Jakob’s early views, a century later, may still provide meaningful clues.

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