Justo Gonzalo's groundbreaking contributions to the study of cerebral functional organisation

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ABSTRACT

The functional organisation of the brain has been studied for many years. Gall was the first to do so, and subsequently, Flourens, Broca, Goltz, Kleist, Lashley, and many other researchers each attempted to tackle this complex problem. In Spain, Justo Gonzalo Rodríguez-Leal (1910-1986) proposed an innovative theory of the functional structure of the cerebral cortex. He presented and developed this theory in his book *Investigaciones sobre la nueva dinámica cerebral. La actividad cerebral en función de las condiciones dinámicas de la excitabilidad nerviosa.* This exceptional theory did not meet with the response it deserved, and his treatise was overlooked for many years. In 1939, Justo Gonzalo identified what he named 'dynamic action phenomena', the starting point for his theory on cerebral dynamics. This discovery was followed by his two principles of cerebral dynamics: the impact of the brain lesion according to its magnitude and position (1941), and sensory organisation according to spiral development (1947). At a later date, in the 1950s, he would develop the concepts of cerebral gradient, similarity, and allometry. This article aims to summarise the research carried out by this forgotten scholar of the human cerebral cortex and its functional organisation.

KEYWORDS
Justo Gonzalo Rodríguez-Leal, cerebral dynamics, functional organisation, gradient, allometry, 20th-century history

Introduction

The functional organisation of the brain was one of the leading topics in the neurophysiology of the 19th and early 20th centuries. The first structured and systematic approach to this subject was delivered by neuroanatomist and physiologist Franz Joseph Gall (1758-1828). Gall stated that just as the body contains organs associated with certain physiological functions, the brain is also made up of 'mental organs', each of which manages a specific task.[1] His views were opposed by Marie-Jean-Pierre Flourens (1794-1867), who defended the cerebral cortex as a single functional unit and disagreed with Gall's anatomo-functional correlations.[2] The concept of the brain as consisting of functionally homogeneous and equipotential tissue was once widely accepted by the scientific community, and it was supported dogmatically during the first half of the 19th century. In the second half of the century, new findings about the neuroanatomical basis of language, and results from cerebral stimulation experiments in animals, would result in a paradigm shift. In 1861, Paul Broca (1824-1880) presented the findings from post-mortem anatomical studies of two patients who had displayed loss of expressive language. In both cases, he observed a lesion located in the third left frontal gyrus; this was the first clinical evidence indicating a link between a single cognitive function and a specific area of the cerebral cortex.[3,4] A few years later, in 1870, Gustav Theodor Fritsch (1838-1927) and Eduard Hitzig (1838-1907) published the first experimental proof to directly locate a function in a specific area of the cerebral cortex (*Archiv für Anatomie und Physiologie*).[5]

By the end of the 19th century, many researchers were drawing 'functional maps' of the cerebral cortex that pinpointed countless mental processes within specific

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areas of the brain. This functional mapping tendency reached what was perhaps its apex with the monumental treatise titled *Gehirnpathologie*, published in 1934 by Karl Kleist (1879-1960).[6] In contrast to the localisationist points of view, such researchers as Constantin von Monakow (1853-1930), Henry Head (1861-1940), and Kurt Goldstein (1878-1965) proposed a holistic view of the brain according to which mental activities are the product of multiple brain areas interacting with each other. Shepherd Ivory Franz (1874-1933) and Karl Lashley (1890-1958) also supported this line of reasoning. The latter both stated that although functional specialisation does exist on the sensory and motor levels, the brain works as a complete unit rather than a collection of parts.[2]

In Spain, Catalan neuroscientist Justo Gonzalo Rodríguez-Leal (1910-1986) would propose an innovative theory about the functional structure of the cerebral cortex. He presented and developed this theory in his book *Investigaciones sobre la nueva dinámica cerebral. La actividad cerebral en función de las condiciones dinámicas de la excitabilidad nerviosa*.[7] Despite being praised by his countrymen and international scholars for his book's originality and scientific relevance,[8] Justo Gonzalo's exceptional insights into the problem of cerebral localisation did not make the impact they deserved, and the treatise remained forgotten or overlooked for a long period of time. Justo Gonzalo's infrequent participation in scientific congresses, his unwillingness to divide his research into small publishable units, the indifference of most of his colleagues, and his own strictness and self-criticism are all factors that explain why his studies remained so obscure.

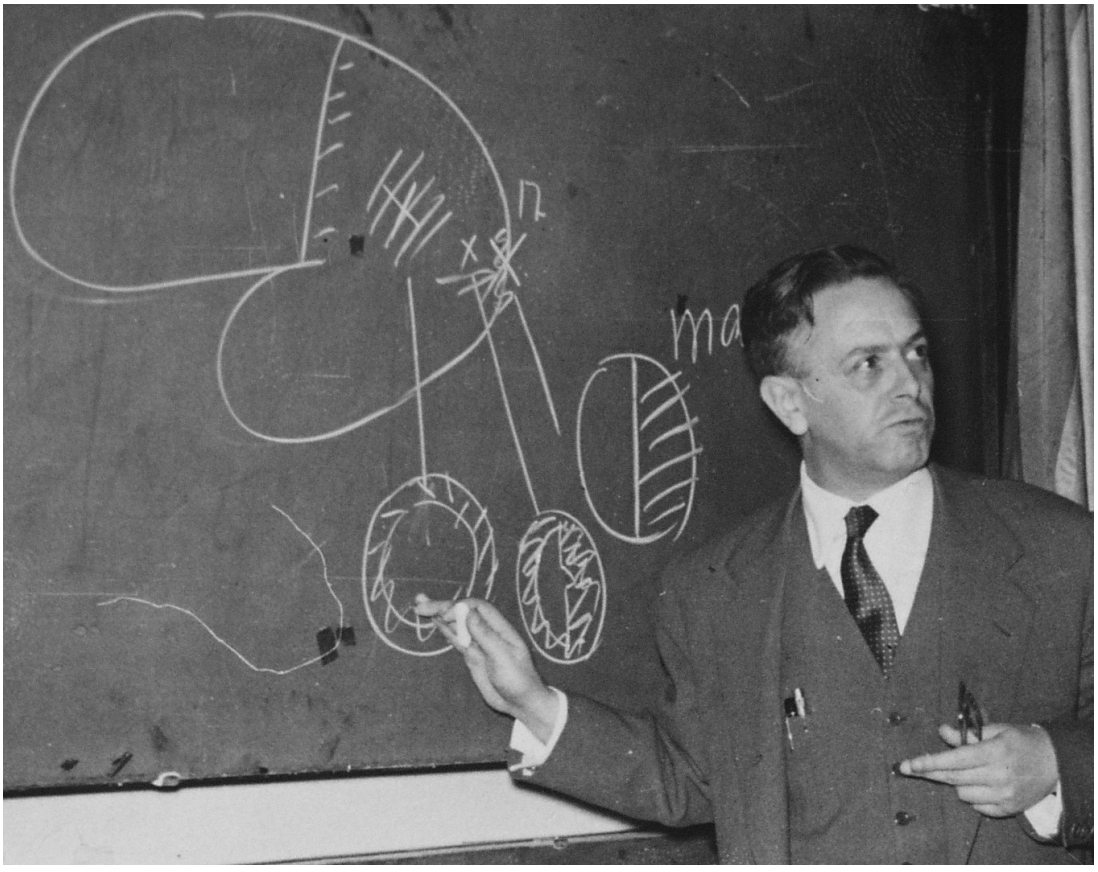

Figure 1. Justo Gonzalo during a lecture on cerebral dynamics. Fourth congress of the Spanish Association of Neuropsychiatry (Madrid, 1954). Personal collection of I. Gonzalo Fonrodona.

Development

Brief biography of Justo Gonzalo

Justo Gonzalo Rodríguez-Leal was born in Barcelona on 2 March 1910, and spent most of his childhood and adolescent years in that city. His family moved several times because of his father's occupation as a civil engineer. Justo first attended secondary school in Valencia but had to finish his course in Barcelona, where he would later enrol in university studies. Shortly thereafter, his father was transfered to the shipyards in Seville; Justo, who preferred to be closer to his family, decided to attend medical school in Madrid. He graduated in 1933 and then completed more specialised courses at the University of Vienna, with Hans Hoff and Otto Pötzl, in the 1933-1934 academic year. A grant from the Board for Advanced Studies (*Junta para la Ampliación de Estudios e Investigaciones Científicas*) allowed him to continue his training at the University of Frankfurt under the eminent German neurologist and psychiatrist Karl Kleist (1934-1935).[9] In partnership with Dr Kliest, Justo Gonzalo published an article on thalamic localisation and physiopathology.[10]

Upon his return to Spain, he attended patients as a consultant neurologist at Madrid's Hospital General (currently the Museo Reina Sofía building) and conducted anatomical and clinical brain research at the nearby Cajal Institute. Soon after the outbreak of the Spanish Civil War (1936-1939), he was sent to the Republican front as a medic in the Communist battalion under the command of Enrique Líster.[11] In the summer of 1938, he managed to be recruited by Gonzalo Rodríguez Lafora to work in the Head Trauma Centre, directed by the latter in Godella, Valencia. After the war, Justo Gonzalo returned to Madrid and presented the initial results from his studies to the Spanish National Research Council (CSIC), whose ranks he joined as a researcher in 1942. He made time for both research and teaching; between 1945 and 1966, he presented doctoral courses in brain physiopathology at Madrid's Faculty of Medicine (a building that had formerly housed Hospital San Carlos). Although he retired in 1980, Justo Gonzalo continued his research until his death on 28 September 1986.[12]

Cerebral dynamics: the background

The information presented in this section is based on Justo Gonzalo's *Investigaciones sobre la nueva dinámica*

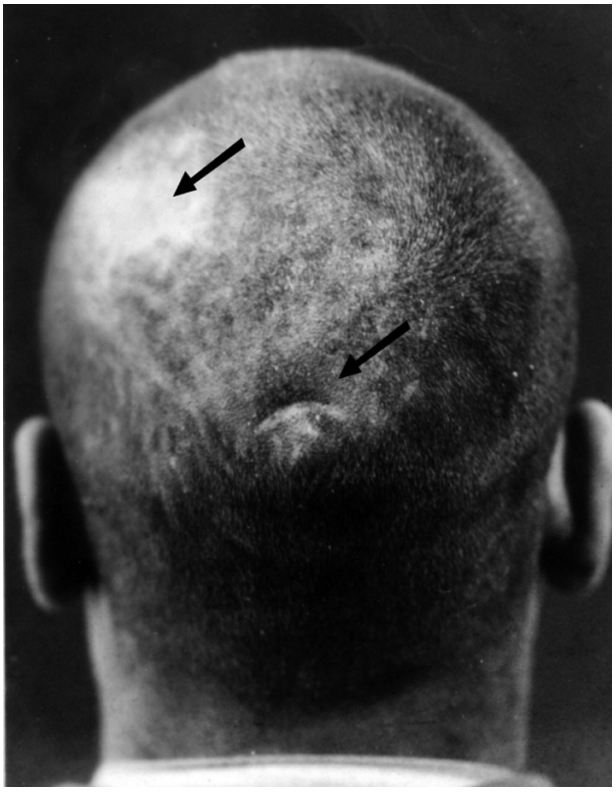

Figure 2. Patient M. Taken from *Dinámica cerebral*[7]

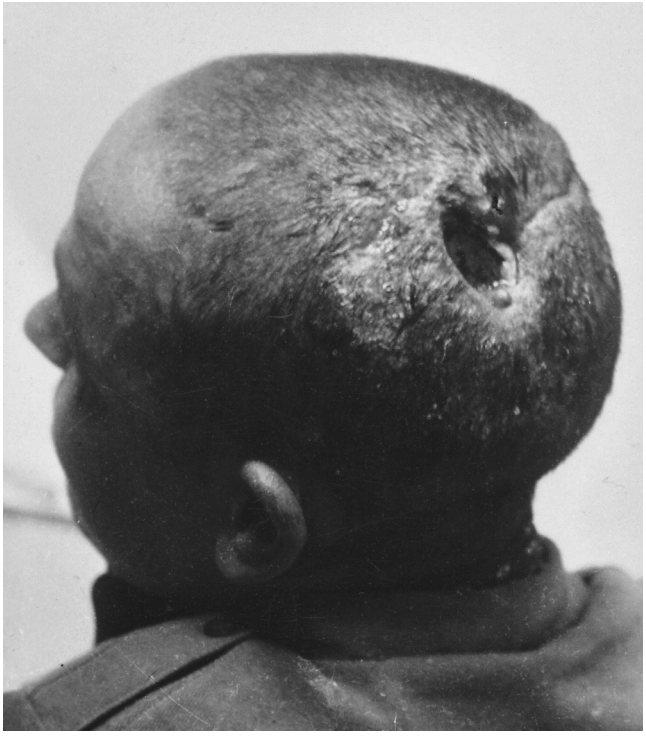

Figure 3. Patient T. Taken from *Dinámica cerebral*[7]

cerebral. La actividad cerebral en función de las condiciones dinámicas de la excitabilidad nerviosa,[7] which provides the full explanation of his theories.

In August 1938, during his stay at the Head Trauma Centre, Justo began researching agnosia. The phenomena he observed as he examined large numbers of patients with traumatic brain injury led him to question the dominant ideas about cerebral disorders. One of his most intriguing cases was patient M, a 25-year-old male who in May 1938 had been struck by a projectile whose impact caused a lesion in the left parieto-occipital region of the brain. As a result of the injury, he presented severe peripheral vision loss, triplopia (triple vision of a single object), distorted chromatic contour perception (seeing colours as detached from objects), abnormal colour perception, visual agnosia, apraxia syndromes, signs of tactile agnosia, and other disorders. One of his most striking symptoms was inverted visual perception (with a maximum perceived tilt of 170º in the left eye and 145º in the right). A meticulous examination carried out at a later date revealed functional separation dependent on the intensity of the stimulus, with tactile and auditory inversion. The patient displayed remarkably accentuated temporal summation and multisensory facilitation (for example, an intense muscle contraction would improve his perception considerably). During his stay in Godella, Justo described another case (patient T) with a brain injury and clinical features similar to those of patient M. This second patient, a 20-year-old man who had been wounded in January 1938, displayed similar injuries to patient M's, although less severe and in a slightly superior localisation. As in patient M, patient T presented loss of upright vision such that he could read normally placed text as well as inverted text without noticing the position of the letters. An in-depth analysis of both cases led Gonzalo to change his theoretical approach to cerebral activity and devise an original model of brain function based on the laws of nerve excitability. In late 1939, he described what he termed 'nervous phenomena of dynamic action', listed as follows: *1)* nerve signal discrepancy or asynchronicity, *2)* synchronisation due to reinforcement or summation, and *3)* repercussion. These phenomena constitute the starting point for cerebral dynamics and the subsequent issue of localising cortical lesions.

According to Justo, the effect of a cortical lesion depends on two factors: magnitude and position. The position or localisation of the lesion will determine how the cerebral disorder is distributed (topography of the repercussion). The lesion magnitude or extension will determine the intensity of the disorder or the degree of functional disability. This last concept lets us envision a transitional continuum for different abnormal phenomena and exclude independent defects. As such, the difference between paralysis and paresis, and between anaesthesia and hypoaesthesia, resides in the degree of impairment of the same function. Lesion location is instrumental in defining three general cortical syndromes: central, paracentral, and marginal. Central syndrome of the cortex is characterised by multisensory impairment (visual, tactile, and auditory) that is bilateral and symmetrical. The syndrome reveals dynamic aspects of integrative brain processing in the progressive loss of sensory ability (depending on stimulus intensity and the volume of neural tissue loss). It also clearly shows that areas are interrelated and highlights the continuous variation in cortical specificity and the role of the cortex as a functional unit. Paracentral syndrome is similar to that described above except that its effects are asymmetrical. A marginal syndrome, in turn, is one affecting the projection pathways (an example of a visual marginal syndrome might be homonymous hemianopsia). Central and paracentral syndromes are accompanied by functional inhibition, whereas marginal syndromes display functional suppression or interruption. In 1952, Justo completed a search for new cases that would help corroborate his working hypothesis. He examined about 100 patients out of a list of 3000 with brain injuries (most of whom were wounded in the Spanish Civil War). Of the examined patients, 35 presented a central syndrome similar to that shown by patients M and T, while another 35 displayed signs of paracentral syndrome.

The two factors Justo indicates –magnitude and position– constitute the doctor's first solution to the complex problem of cerebral localisation. Ten years later, in 1951, he formulated a new approach to this problem that incorporated the concept of gradient (understood as the proportion by which a magnitude varies with distance). In contrast with the concept of the cerebral cortex as parcelled out into a mosaic of anatomical centres, Justo postulated that the cortex consisted of multiple cerebral gradients displaying functional continuity. Within this system of cerebral gradients, it is possible to distinguish between specific gradients (which involve the factors of magnitude and position mentioned above) and gradients of integration (the result of intersections between specific

gradients). According to localisationist theories, brain injury destroys anatomical centres, and with them, their specific functions. In Justo's view, however, the pathological changes observed after brain injury were the result of an array of gradients; the system as a whole preserves its functional organisation, but its myriad functions are affected by a change in the scale of nerve excitability. According to the principle of dynamic similarity, a change in a system's scale gives rise to different rates of change among its components (allometric scaling relations). In this new view of cerebral dynamics, cerebral gradients indicate the localisation of different systems, whereas dynamic similarities and allometry reveal their functional pathways. On the other hand, the cerebral gradient concept pared down the classic distinction between projection and association zones, and with it, the distinction between higher and lower mental functions. Continuity is provided by means of a single functional pattern that sets the scene for later stages of increasing complexity.

Justo Gonzalo's concept of cerebral dynamics would evolve considerably over a period of more than four decades. This idea began to take shape in 1939 with his studies of dynamic action phenomena. This was followed by his two principles of cerebral dynamics: the impact of the brain lesion according to its magnitude and position (1941), and sensory organisation according to spiral development (1947). At a later date, in the 1950s, he would develop the concepts of cerebral gradient, similarity, and allometry. In one of his last definitions of cerebral dynamics, Justo Gonzalo described it as "an acquired local pattern of allometry gradients". This refers to the neurophysics of the cerebral cortex, a system arranged in a gradient field. While brain lesions change the metric scale, the brain preserves its plan or model and functional similarity; its many particular functions are defined and managed allometrically.[7(p73, suppl.II)] Recently published papers have mentioned the concepts developed by Justo Gonzalo and applied them to the modern context.[13,14]

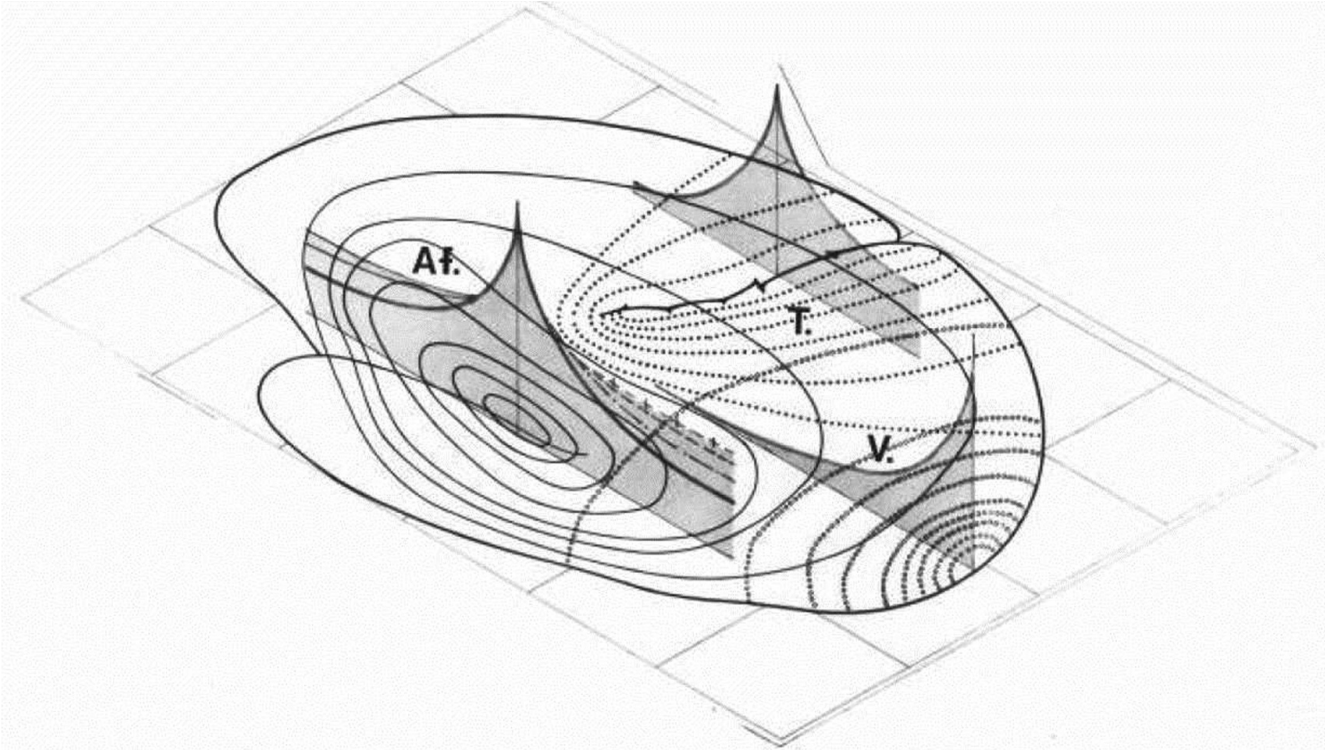

Figure 4. Aphasia gradient (Af), tactile gradient (T), and visual gradient (V). Taken from *Dinámica cerebral*[7]

Conclusions

Historically, scholars of functional cerebral organisation have identified as either localisationists or anti-localisationists (holistic theoreticians). The cerebral dynamics model proposed by Justo Gonzalo may actually bridge the gap between these two positions and integrate their respective theories. According to Cabaleiro Goas, cerebral dynamics completes and polishes localisationist theory rather than refuting it.[8] Justo himself stated that

> "the cerebral dynamics model is connected to the previous [theories]. In addition to being a physiological reality, it still pertains to clinical anatomy and therefore includes anatomical concepts (cerebral hemispheres, corpus callosum, primary and secondary areas, intersections, etc.); physiological concepts (excitability, summation, phase shifts, sensory dimensions, cerebral gradients, etc.); and pathophysiological concepts (central, paracentral, and marginal syndromes, the residual field, spiral development, etc.)".[7(p63, suppl.I)]

If we were to establish parallels between Justo Gonzalo's work and that of an earlier scholar, Henry Head or Karl Lashley might be good candidates. From within their respective disciplines, both of these researchers were vocal critics of the anatomical and static positions defended by the localisationists. They supported a dynamic and integrative view of brain function. Henry Head's conception of the cerebral cortex resembled a mosaic made up of integration foci. Showing the influence of Sir Charles Scott Sherrington's integrative view of the nervous system, Head argued that a focal brain lesion created a disturbance throughout the entire brain. He proposed that a brain that had undergone damage should be regarded as a completely new system, not just the former system with a new deficit in the region or regions anatomically affected by the lesion.[15] In *Brain mechanisms and intelligence* (1929), Karl Lashley affirms that functional brain structure is not the sum of a series of specific and anatomical centres, but rather the dynamic organisation of the cerebral system viewed as a whole.[16,17]

This dialectic clash between localisationists and anti-localisationists is still in evidence today. The clinical sphere includes many doctors with a more modular view of cerebral architecture. In 1952, Justo Gonzalo observed that "the traditional doctrine [of anatomical localisations] is still at work, in one way or another, in clinical diagnosis".[7(p63, suppl.I)] Today, it would be a mistake to adopt excessively static and compartmentalised perspectives to the concept of brain activity. A better option would be to follow the lead of Justo Gonzalo Rodríguez-Leal in seeking a more overarching, dynamic, and integrated view of the brain's functional organisation.

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