Chronology of Justo Gonzalo's research on brain dynamics

Alberto García-Molina, Isabel Gonzalo-Fonrodona

Introduction. The Spanish neuroscientist Justo Gonzalo y Rodríguez-Leal (1910-1986) investigated the functional organisation of the cerebral cortex over more than four decades. His findings led him to formulate a neurophysiological theory based on the laws of nervous excitability, which he called brain dynamics. This paper presents in chronological order how the main ideas on which it is based arose.

Development. In 1939, Gonzalo observed the phenomena of dynamic action: asynchrony or disaggregation, facilitation and cerebral repercussion. This was followed by two principles: the cerebral effect of lesions according to their magnitude and position (1941), and spiral development of the sensory field (1947). At the same time, he characterised what he called the central syndrome of the cerebral cortex. In the 1950s he developed the concepts of the cortical gradient, similarity and allometry. In contrast to modular conceptions of the cerebral cortex, in which one region is responsible for one function, Gonzalo argued that 'cortical gradients provide the location of systems, while similarity and allometry reveal their functional mechanism.'

Conclusions. The theory of brain dynamics was established in two stages. The first (between 1938 and 1950) had an important clinical foundation, involving the observation of new phenomena and the formulation of new concepts. The second (between 1950 and 1960) included the introduction of more far-reaching concepts, such as the functional cortical gradient, and allometry laws based on a change of scale. Today, various authors believe that the concept of the gradient is crucial for understanding how the brain is organised.

Key words. Brain dynamics. Central syndrome. Cortical gradient. Facilitation. Inverted perception. Multisensoriality.

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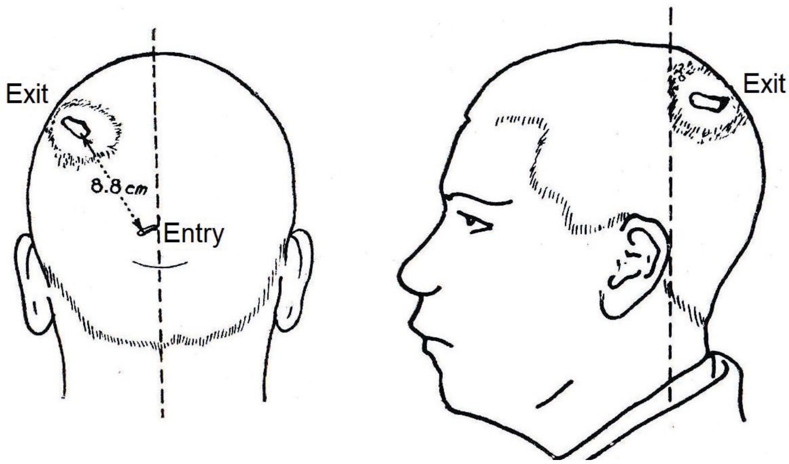
Introduction

At the end of the 18th century, Franz Joseph Gall proposed that the brain is made up of mental organs, each of which with a specific function. Gall's *Schädellehre* (doctrine of the skull), although erroneous in its methodology, forced a rethinking of brain physiology, associating mental functions with specific areas of the cerebral cortex. Pressures of different kinds favored the decline of the Schädellehre and the rise of the hypothesis that all cortical regions are functionally equipotential[1]. The modular conception of the cerebral cortex, far from disappearing, was reborn in the sixties of the 19th century thanks to Paul Pierre Broca. In 1874, Carl Wernicke enriched the localizationist doctrine and proposed that mental functions are not the property of specific cortical regions, but emerge from anatomical connections between them [1,2].

The localisationist-connectionist doctrine became the frame of reference of neurology and neurophysiology of the last third of the 19th century and the first of the 20th century. However, there is no lack of authors who rejected the anatomical (static) criterion and defended and advocated a dynamic approach to cortical functional organisation. Von Monakow, for example, argued that the brain is organised in constellations of temporally synchronised networks [3], while Jacob argued that psychic process is generated by dynamic interfocal and transfocal combinations [4]. In the late 1930s, Justo Gonzalo in Spain proposed a physiological and dynamic understanding of the brain that gave rise to a conception based on the laws of nervous excitability. It was presented in his extensive two-volume monograph [5,6], two extensive articles [7,8], various unpublished writings and later diagrams. The novelty and importance of this research was noted at the time by several authors [9-17]. Others, such as Piéron, Katz, Buscaino, Bing and Köhler, expressed their interest through personal letters to Gonzalo [18-22]. The research was largely silenced with the death of several authors of that time because the monograph, which was soon out of print, was neither reprinted nor translated, and the author's publications were not published in in-

Figure 1. Patient M. Schematics showing the entry and exit scars caused by the projectile. Their location suggests lesions in the left parietooccipital convexity. (Figs. 1 and 2 from [7]).



ternational journals. However, in the 1970s, it continued to be commented on by Spanish authors such as Ballús [23], Llopis [24] and Roldán [25], among others. Shortly afterwards, it had considerable impact on the field of cybernetics and artificial intelligence [26,27]. In the 21st century, the author Gonzalo and his singular work have been studied historically by authors such as Barraquer-Bordas [28] and García-Molina [29].

The aim of this paper is to present a chronological overview of the development of Gonzalo's theory of brain dynamics through an analysis of his publications and unpublished documentation from the family archive, and finally to highlight its current relevance.

First stage (1938-1950)

Dynamic action phenomena

In early 1938, during the Spanish Civil War, Gonzalo was assigned to a Military Health Hospital in Godella, (Valencia, Spain) where, both in this hospital and in the General Hospital of Valencia, he had the opportunity to examine a large number of patients with brain injuries [30,31]. Among them, a soldier with a lesion in the left parietooccipital convexity (patient M; Fig. 1) was particularly noteworthy [32]. His particular symptomatology led Gonzalo to question the prevailing knowledge on brain pathology.

When Gonzalo examined patient M, who seemed to show only an intense concentric reduction of the visual field, he noticed the presence of a chromatic disturbance that made him see colours as if they were detached from objects, a disturbance known as 'flat colour' perception [33]. The patient also presented a lack of perception of motion and other gnostic disturbances. A couple of months later, he found by chance that the patient saw objects tilted and even almost inverted if they were sufficiently distant, or if their size, illumination or exposure time was reduced. These disturbances went unnoticed at first glance, as they did not seem to disturb the patient's daily behaviour. In another patient, T, with a smaller lesion in the same area, the visual image was tilted only about 30° when the object was moved away [5,34]. A remarkable peculiarity in both subjects was that they read texts in different orientations (right and upside down) without noticing any difference.

Gonzalo's in-depth analysis at the end of 1939 led to the unexpected discovery in patient M of what he called 'dynamic action' phenomena, in which the physiological criterion of excitability became indispensable. This was a radical change in the usual concepts and made it possible to plan a detailed study of M and T. These phenomena are [5,34]:

- *Asynchrony (or disaggregation)*: splitting (or disaggregation) of sensory phenomena that normally present as all-or-nothing, and which pathologically appear as partial reactions or incomplete phases of response to a stimulus when its intensity decreases. According to Gonzalo, this phenomenon involves an asynchronism of the nervous elements[2].
- *Facilitation and summation*: partial disappearance of disorders in such a way that the perception of a stimulus improves in the presence of another stimulus of the same or a different sensory modality, or by a motor stimulus, or by intensification of the stimulus, or by temporal summation (iteration). This phenomenon was discovered when M's visual perception improved markedly from lying down to sitting or standing.
- *Cerebral repercussion*: this means the alteration of all functions, from simple excitability to the most complex functions, bilaterally and symmetrically, and in all sensory systems.

Cerebral repercussion is the phenomenon of dynamic action that is most opposed to cortical localisation theories[3]. The cerebral repercussion, together with the functional simplification derived from nervous asynchronism, gave rise to what Gonzalo called 'dynamic reduction' of all sensory systems.

In 1941, Gonzalo presented to the Consejo Superior de Investigaciones Científicas (CSIC) (Spanish National Research Council) the unpublished report *Investigaciones sobre dinámica cerebral. La acción dinámica en el sistema nervioso. Estructuras sensoriales por sincronización cerebral* (Research on brain dynamics. Dynamic action in the nervous system. Sensory structures by cerebral synchronization) [34]. In this report, the phenomena of dynamic action are described, together with various measurements of brain excitability in which the increase in reaction time and the asynchrony of the nervous elements are shown. All this is subsequently published and expanded with new experiments and phenomena [5].

Brain dynamics principles and the central syndrome

As a result of the comparison between the M and T cases and the study of other cortical lesions, Gonzalo established in 1941 the first principle of brain dynamics, which states that the effect of a cortical lesion depends on two factors: its magnitude and its position. The position or location of the lesion determines the type of distribution of the disorder in the brain system (the topography of the cerebral impact). The magnitude or extent of the lesion determines the intensity of the disorder, i.e. the degree of functional decrease in the so-called dynamic reduction (degree of the cerebral impact). It follows from this principle that, rather than there being specific centres, there are dynamic effects depending on the magnitude and position of the lesion.

Based on this first principle of brain dynamics, Gonzalo formulated the central syndrome of the cerebral cortex (Fig. 2). He called it central because the lesion is located 'centrally' or equidistant from the visual, tactile and auditory projection areas, and affects these sensory systems equally. At first sight, as Gonzalo pointed out, this syndrome shows little symptomatology, but its detailed study allows us to penetrate the sensory structures through the aforementioned phenomena of dynamic action. Cases M and T are cases of central syndrome of different intensity. Gonzalo also concluded that Goldstein and Gelb's Schneider case [35,36] is a case of central syndrome of intermediate degree between M and T [5,6].

The central syndrome is opposed to the peripheral or marginal syndrome. This syndrome is caused by lesions in the cortical projection areas (whether visual, tactile or auditory) and results in the well-known contralateral alterations of a single sensory system. In terms of vision, this syndrome can manifest as hemianopsia, or as a central scotoma when the lesion is very circumscribed to the occipital pole [8]. Paracentral syndromes are similar to the central syndrome but with an asymmetric repercussion or distribution. Depending on the location of the lesion, three paracentral syndromes can be distinguished: visual, tactile and auditory. In general terms, as the lesion shifts from the central area of the cerebral cortex to the marginal area (projection area), the cerebral impact decreases, and the disorder shifts from being bilateral and general to being restricted to a single sensory system in its contralateral half. This syndromic view contrasts with the modular approach of the localisation theory that

Figure 2. Some of the cases described by Gonzalo. 1) central syndrome; 2) paracentral visual syndrome, and 3) central scotoma (belonging to a peripheral or marginal syndrome) associated with a lesion located in the occipital pole. In the latter cases, there are lesions that go beyond the occipital pole and therefore affect other areas of the visual field [8]. (Fig. 19 from [8]).

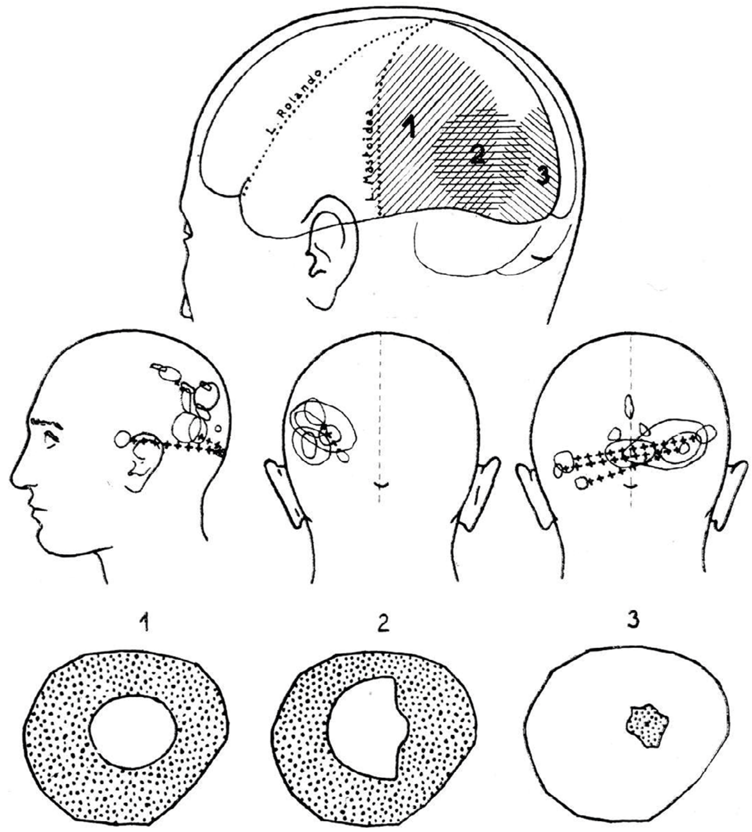
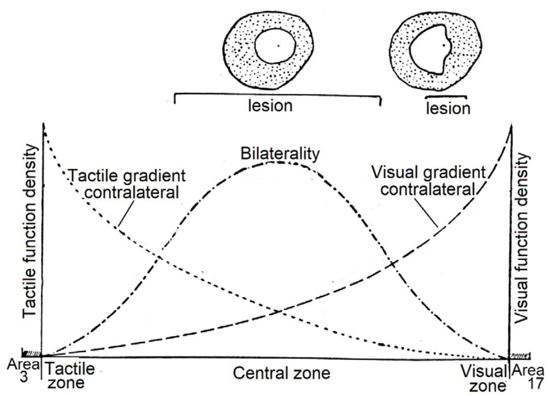


Figure 3. Diagram of cortical gradients. The curves that take a maximum value in the visual and tactile projection area represent respectively the densities of visual and tactile function (specific gradients). The central bell-shaped curve represents the bilateral action by the corpus callosum and the multisensoriality due to the overlapping of the specific gradients. The sizes (magnitudes) of the lesions causing the reduction in the visual fields shown are indicated at the top. (Adapted from figure 20 in [8]).



conceives syndromes as isolated or independent units in which only the cases called by Gonzalo 'marginal' fit. In 1945, all findings together with the examination methods are described in detail in the first volume of the monograph *Dinámica cerebral* (Brain Dynamics) [5]. The first part gives an overview of the phenomenology of the central syndrome and then focuses on the study of visual functions in this syndrome. The following year he discovered tactile and auditory inversion in patient M, with similar characteristics to visual inversion. Spatial inversion is thus generalised in the central syndrome, under minimal stimulation [6,8,37,38]. As the intensity of the stimulus decreases, the inversion process coupled with the dynamic reduction that occurs follows a spiral process, since in the inversion phase there is a marked deviation towards the midline of the body, or centre of the visual field in peripheral vision [6-8]. This discovery led Gonzalo to establish in 1947 the second principle of brain dynamics: the sensory field grows in a spiral development as the stimulus increases.

In 1950 he published the second volume of the monograph *Dinámica Cerebral*, devoted to the analysis of the sensory dynamics of tactile functions in the central syndrome, from elementary sensitivity to bodily and tactile agnosia, and to the extension of concepts [6].

Second stage (1951-1960)

Functional cortical gradients

In 1951, Gonzalo introduced the concept of cortical gradient, whose origin is the aforementioned first principle of brain dynamics. In 1952 he published it in a long article in which he described new cases of central, paracentral and marginal syndrome, choosing the visual field as a reference element [8]. He observed that the 'extra-visual' cortex is involved in the formation of the visual field. This finding led him to question the separation between projection and association areas[4] and to propose a functional continuity across the different cortical regions, admitting, however, differences between them. This led him to the concept of functional gradient, represented by a graded function across the cerebral cortex, which is consistent with the observed transition between different cortical syndromes.

In the case of the visual gradient, for example, the density of visual function is highest in the projection area and decreases progressively towards more central areas of the cortex, with the end of the decline reaching other projection areas. For the visual field to have normal extension, normal acuity, etc., the action of the area of highest density is not sufficient, but the action (integration) of the whole gradient is necessary (Fig. 3). Similarly, Gonzalo proposes the existence of a tactile gradient. Thus, the tactile projection area has some effect on vision, and vice versa. These specific types of gradient have a contralateral character. The bell curve in figure 3 presents an area of overlap of the specific gradients where the unspecificity, i.e. multisensoriality, is maximal. Thus, depending on the position of the lesion, there are multiple types of syndrome: central, paracentral, marginal (or peripheral) and their intermediate transitions, with the intensity of involvement depending on the magnitude of the lesion. In this way, gradients combine the factors of magnitude and position, thus incorporating the first principle of brain dynamics.

In his 1952 article, Gonzalo also points out that a sensory function originating in the projection area (visual, tactile, auditory) is only an inverted and constrained outline that must be elaborated (integrated), i.e. magnified and re-inverted throughout the cerebral cortex. If the lesion is in the projection area, the function is suppressed, but if the lesion is more central, integration is not complete and the central syndrome (functional depression) is produced. In the same article, Gonzalo relates the inversion process to an asynchronism between the primary and secondary areas. The spiral development (second principle) corresponds to the integrating process of the gradient from the projection area to the central zone and beyond. The degree of development depends on the recruited brain mass and can be characterised by quantitative parameters such as intensity, space and time. The marginal zone (projection area) where the specific gradient is maximal is highly differentiated and specialised, and the nervous activity has an anatomical representation, whereas in the central zone, the activity is less organised and its mass has an adaptive or learning capacity. Gonzalo extended the gradient concept to other sensory systems as well as the motor system, and by 1970 he extended it to language [39].

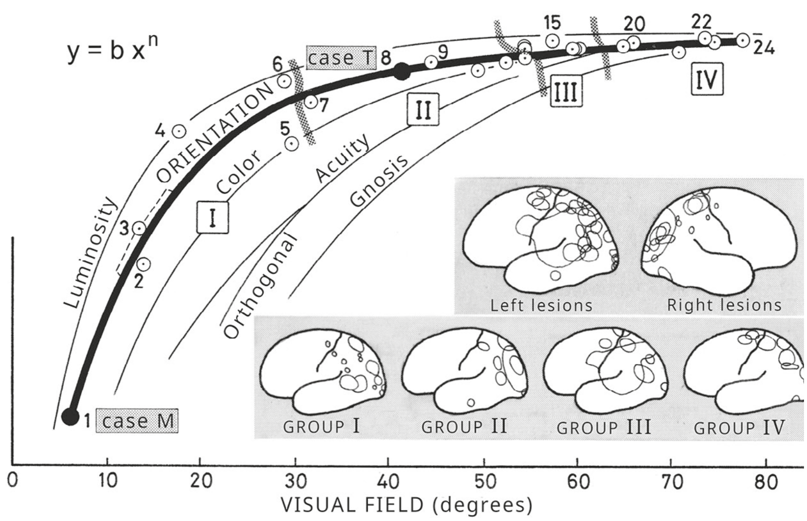
Throughout 1952 and 1953 Gonzalo selected and examined about 200 of the 2.500 brain injured who were part of the registry of the Benemérito Cuerpo de Mutilados de Guerra por la Patria (Meritorious Corps of the Disabled of War for the Fatherland). He carried out the examinations in the brain pathophysiology laboratory of the former Faculty of Medicine in Madrid [40]. As a result, he collected a total of 35 cases of central syndrome and as many cases of paracentral syndromes [39].

Similarity and allometry

In the second half of the 1950s, Gonzalo developed two new fundamental concepts in his conception of brain dynamics: similarity and allometry [39].

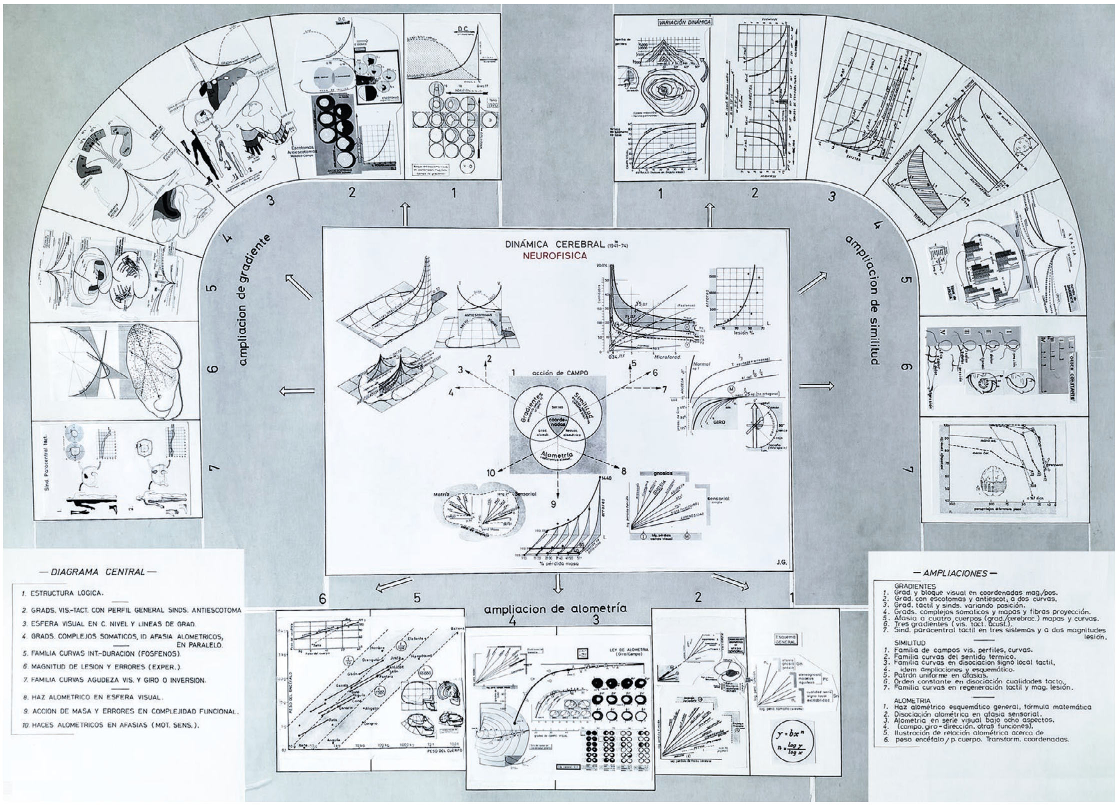
Already in the article published in 1952 he describes more than 20 cases with chronic visual image tilt disorder in various degrees, and arranges them following a curve that correlates the degrees of visual image tilt (image orientation) with the corresponding visual field size [8]. In 1956 he added to this curve other curves for luminosity, colour, acuity and gnosis, which show different (allometric) correlations with the visual field size (Fig. 4). These curves roughly follow functions of the type $y = b\,x^n$ where y denotes the different functions (acuity, orientation, colour, etc.), x is related to the size of the visual field and n (positive number less than unity) is the allometric coefficient, which is different for each function. From figure 4 it can be seen that for a given case with a given visual field size, the visual functions are sorted from the least developed (most affected) to the most developed (least affected) as follows: gnosis, acuity, colour, image orientation and luminosity. This sequence is always the same, and depends on the excitation needs of each of the functions, which are differentially affected by the general excitability deficit [39]. This shows the asynchrony that gives rise to the above-mentioned dynamic phenomenon of the gradual loss (disaggregation) of functions, including the image orientation function.

Figure 4. Allometry. Correlation curves of various visual perceptual functions (luminosity, image orientation, colour, visual acuity and gnosis) with the size of the visual field in 24 cases examined by Gonzalo. The cases are classified into four groups, from most affected (group I) to least affected (group IV). (Fig. 19 from Suppl. II of [39], English edition, with the permission of RTNAC, USC and CSIC).



The allometric relations mentioned (Fig. 4) can be directly deduced from the concept of dynamical similarity, a concept that is specific to dynamical systems; however, Gonzalo did not use such a concept until 1959, although it is already in germ in texts written in 1943 and in his publications [5-8]. He proposes in these works that there is a change of scale in the excitability of the central syndrome with respect to a normal subject, and between central syndromes of varying magnitude. It is suggested that the functional depression in the central syndrome results from a new brain balance that maintains the same type of organisation: the functions follow the same laws as in the normal subject but varying the parameters according to the number of neurons remaining. As Gonzalo states, 'cortical gradients give the localisation of systems, whereas similarity and allometry reveal their functioning' [39].

Figure 5. General diagram of brain dynamics, by Gonzalo in September 1977. Illustrations on gradients (top left), similarity (top right), allometry (bottom), and synthesis in the centre. Reduced photograph of the original with Spanish text. (Family archive of J. Gonzalo).



Last modifications (1960s and 1970s)

In the 1960s, Gonzalo refined the concepts of gradient, similarity and allometry, and in 1970 he extended them to language [39] (Fig. 5, box 5 on the right). Simultaneously, he recovered the concept of change of scale in the excitability of the system in the central syndrome, but this time as a basic concept from which the dynamic similarity is automatically deduced, and from it, the allometric variation of the different functions of the system is obtained. This explains the phenomenology of the central syndrome. He arrived at this result through the study of dynamic systems and, in particular, of biological systems and the laws governing their growth. A remarkable aspect of the central syndrome is that the organisational plan is similar to that of healthy subjects, except that the deficit of excitability (and integration) reveals the organisation of the sensory functions since they are disaggregated [39,42].

In a document written around 1975, Gonzalo wrote: 'The brain dynamics developed (...) constitutes a neurophysics of the cerebral cortex; it would be a system with gradient fields, which changes the metric scale in lesions but preserves the same organization, or functional similarity, and whose multiple particular functions are specified allometricaly governed by allometric coefficients' [39].

Concluding remarks

The two principles of brain dynamics, formulated in the first stage of brain dynamics theory (1938-1950), attempt to answer similar physiological questions and constitute Gonzalo's first approach to the complex question of cortical functional organisation. In the first principle, the magnitude of the lesion is related to the degree of global brain involvement (linked to holistic or functional theories); the position advocates local action (somewhat reminiscent of localisationist theories). In the second principle, spatial inversion conforms to anatomical location or configuration, whereas magnification and re-inversion (reorganisation) are connected to holistic theories.

The formulation of the concept of functional cortical gradient marks the beginning of the second stage of brain dynamics (1951-1960). In contrast to the parcellation of the cerebral cortex as a 'mosaic' of static centres, characteristic of the localisationist-connectivist theory, Gonzalo proposed multiple cortical gradients with functional continuity and regional variation. This represents, using Gonzalo's terms, a system of quantitative localisations according to fields of action, in such a way that at each point, the combination of the specific factor with the non-specific multisensory factor confers on that point properties different from those of the other points.

Gonzalo's cortical gradient is not fully understood at a time when the more accessible and conceptually simple notion of modularity was the paradigm of reference for understanding and explaining the functioning of the cerebral cortex. With the exception of the contributions of Teuber [43] and Goldberg [44,45] in the last third of the 20th century, it is not until the 21st century that several authors consider the concept of gradient to be one of the essential principles of brain organisation [46-50]. Similarly, the dynamic phenomenon of multisensory facilitation started to be discussed in detail at the end of the 20th century and is now a very active field of research [51-56], although motor facilitation is hardly known. It is worth noting that in Gonzalo's model, gradients are closely related to multisensory processes, shedding light on these processes.

Notes

1. In the 18th century, Emanuel Swedenborg (1688-1772) proposed, on a theoretical level, the notion of cortical localisation. The parcellation of the cerebral cortex in functional regions is a legacy of the scientists of the 19th century.
2. In the unpublished memoir of 1941, Gonzalo uses the word heterochronaxy as a synonym for asynchronism [34]. In 1909, Louis Lapicque introduced the term chronaxia to describe the duration of a stimulus capable of eliciting the minimum motor response (threshold) at twice the intensity of the rheobasee (intensity capable of eliciting a minimum motor response).
3. The cerebral repercussion is, in a sense, a permanent diaschisis, in contrast to the concept of transient diaschisis associated with acute brain injuries, a term introduced by Constantin von Monakow in the early 20th century.
4. In 1939, Jakob also rejected the division of the cerebral cortex into separate areas of projection and association. He argued that gnosis and praxis are neither sensory nor motor but concomitantly sensorimotor processes [4].

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Cronología de la investigación sobre la dinámica cerebral de Justo Gonzalo

Introducción. El neurocientífico español Justo Gonzalo y Rodríguez-Leal (1910-1986) investiga la organización funcional de la corteza cerebral durante más de cuatro décadas. Sus hallazgos le llevan a formular una teoría neurofisiológica basada en las leyes de la excitabilidad nerviosa, que denomina dinámica cerebral. En el presente trabajo se expone de forma cronológica cómo surgen las principales ideas sobre las que se articula.

Desarrollo. En 1939 Gonzalo observa los denominados fenómenos de acción dinámica: desfasamiento, facilitación y repercusión cerebral. Le siguen dos principios: efecto cerebral de la lesión según la magnitud y posición (1941), y organización sensorial, según un desarrollo espiral (1947). Paralelamente, caracteriza lo que llama el síndrome central de la corteza cerebral. En la década de los cincuenta desarrolla los conceptos de gradiente cortical, similitud y alometría. En contraposición a las concepciones modulares de la corteza cerebral, en las que una región es responsable de una función, Gonzalo expresa que 'los gradientes corticales dan la localización de los sistemas mientras la similitud y alometría revelan su trama funcional'.

Conclusiones. La teoría de dinámica cerebral se articula en dos etapas. La primera (de 1938 a 1950) se caracteriza por una importante base clínica con observación de nuevos fenómenos y formulación de nuevos conceptos. La segunda (de 1950 a 1960) incluye la introducción de conceptos de mayor alcance, como el gradiente funcional cortical, y leyes de alometría que se basan en un cambio de escala. Actualmente, varios autores consideran que el concepto de gradiente es clave para entender la organización cerebral.

Palabras clave. Dinámica cerebral. Facilitación. Gradiente cortical. Multisensorialidad. Percepción invertida. Síndrome central.