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A re-examination of neural basis of language processing: Proposal of a dynamic hodotopical model from data provided by brain stimulation mapping during picture naming

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ABSTRACT

From recent findings provided by brain stimulation mapping during picture naming, we re-examine the neural basis of language. We studied structural–functional relationships by correlating the types of language disturbances generated by stimulation in awake patients, mimicking a transient virtual lesion both at cortical and subcortical levels (white matter and deep grey nuclei), with the anatomical location of the stimulation probe. We propose a hodotopical (delocalized) and dynamic model of language processing, which challenges the traditional modular and serial view. According to this model, following the visual input, the language network is organized in parallel, segregated (even if interconnected) large-scale cortico-subcortical sub-networks underlying semantic, phonological and syntactic processing. Our model offers several advantages (i) it explains double dissociations during stimulation (comprehension versus naming disorders, semantic versus phonemic paraphasias, syntactic versus naming disturbances, plurimodal judgment versus naming disorders); (ii) it takes into account the cortical and subcortical anatomic constraints; (iii) it explains the possible recovery of aphasia following a lesion within the "classical" language areas; (iv) it establishes links with a model executive functions.

1. Introduction

For more than a century, lesion studies on aphasiology have led to a localisationist view of language organization, in which Broca's and Wernicke's areas are assigned the leading roles in language production and comprehension, respectively. Nonetheless, anatomo-functional correlations based on lesion method suffer from many limitations. The first is the size of the injuries, which are often extensive, especially in stroke. Secondly, the accurate three dimensional delineation of damages was very difficult until development of MRI. Indeed, recent MRIs of Leborgne's and Lelong's brain showed wide injuries involving not only the classical "Broca's area" but also the insula and perisylvian white matter (Dronkers, Plaisant, Iba-Zizen, & Cabanis, 2007) – meaning that the "motor aphasia" did not necessarily result from lesion to the inferior frontal operculum. Thirdly, in lesion maps, it is dangerous to interpret that a "statistical epicenter" common to every patients is the region which sub-served the disturbed function. In fact, the same neurological deficit may be due to damages in different locations across patients, all of them being involved in a large functional network around (but not including) the "epicenter" thought to be crucial. Finally, compensatory mechanisms of post-lesional plasticity can also occur, especially in slow-growing lesions (Desmurget, Bonnetblanc, & Duffau, 2007; Duffau, 2005).

Advances in functional neuroimaging have recently enabled to provide new insights into the neural basis of language, both in aphasic patients and healthy volunteers (Vigneau et al., 2006). Nonetheless, it is worth noting that these techniques, even if they do not have the pitfalls of lesion method, are based on the principle of "activations" during task performance and paradoxically lost the major advantage of lesion studies, that is, the correlation of structure with functional disturbances. In other words, it is not because an area has been activated on fMRI that its destruction will cause a deficit.

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Here, our goal is to re-examine the neural foundations of language on the basis of data issued from direct electrical stimulation (DES) of the brain in awake patients. Indeed, during surgery for a lesion (such as a tumor) invading both cortical and subcortical structures, it has become common clinical practice to awaken patients in order to assess the functional role of restricted cerebral regions (the brain has no receptors for pain). The surgeon can maximize the extent of resection, and thereby improve the overall survival, without generating functional (especially language) impairments, thanks to an individual mapping and preservation of eloquent structures: it means that the resection is performed according to functional boundaries (Duffau, 2007; Duffau, Gatignol, Mandonnet, Capelle, & Taillandier, 2008). Concretely, patients perform several language tasks, such as counting or picture naming, while the surgeon temporarily interacts with discrete areas within the grey and white matter around the tumor, using DES. If the patients stops speaking or produces wrong response, the surgeon avoid removing the stimulated site (Duffau, 2011; Duffau et al., 2002). Although the exact mechanism of DES remains unknown, the usual view is that DES transiently interacts locally with a small cortical or axonal site, but also non-locally, as the focal perturbation will indeed disrupt the whole (sub-)network sustaining a given function (Mandonnet, Winkler, & Duffau, 2010). Therefore, conversely to functional neuroimaging, DES induces a transient virtual lesion, by inhibiting a sub-circuit during approximately 4 s, with the possibility to check whether the same language disorders are reproduced when repeated stimulations are applied over the same area. Interestingly, by gathering all cortical and axonal sites where the same type of errors have been observed when stimulated, one would build up the sub-network of the disrupted subfunction. As a consequence, DES was extensively demonstrated to represent a unique opportunity to identify with a great accuracy (about 5 mm) and reproducibility, in vivo in humans, the structures that are crucial for cognitive functions, especially language, both at cortical and subcortical (white matter and deep grey nuclei) levels. In addition, combining language disturbances elicited by intrasurgical DES with the anatomical data provided by pre- and post-operative MRI has enabled to perform reliable anatomo-functional correlations (Duffau, 2011; Duffau et al., 2002).

We will review the original data provided by intraoperative DES during awake surgery within the left dominant hemisphere to propose a revisited model of language, switching from a modular to a hodotopical (delocalized) and dynamic view, in which language is conceived as resulting from parallel processing performed by distributed groups of connected and synchronized neurons, rather than by individual centers (Duffau, 2008). In this framework, language is underlain by large-scale sub-networks interacting together and able to compensate themselves after brain lesion (at least to some degrees), opening the door to brain plasticity. In pathology, according to this new concept, a topological mechanism (from the Greek *topos* = place) refers to a dysfunction of the cortex (deficit, hyperfunction or a combination of both), whereas a hodological mechanism (from the Greek *hodos* = road or path) refers to dysfunction related to connecting pathways (disconnection, hyperconnection or a combination of both) (Catani, 2007; de Benedictis & Duffau, 2011). In other words, it is mandatory to take into account the complex functioning of a wide distributed circuit to understand both its physiology as well as the functional consequences of a lesion of this network – with possible distinct deficits depending on the location and the extent of damage (e.g. purely cortical, or purely subcortical, or both).

Of note, the picture naming task has extensively been used in the literature for intraoperative language mapping in awake patients (Ojemann, Ojemann, Lettich, & Berger, 1989; Sanai, Mirzadeh, & Berger, 2008). Indeed, this is a very sensitive test which involves a large network, thus adapted for the surgical conditions, due to the limitation of time for mapping (about 2 h). Consequently, we will take picture naming as main paradigm in our review, even if other tasks will be considered throughout the manuscript. In a first part, we will correlate the different types of errors elicited by DES stimulation during a picture naming task with the "classical" LRM model of spoken word production (Levelt, Roelofs, & Meyer, 1999) which will serve as a reference. In a second paragraph, we will study structural–functional relationships by correlating the types of language disturbances generated by DES with the anatomical location of the stimulation probe. From these original data, we will show that the serial LRM model cannot explain all the symptoms elicited by DES, and we will propose an alternative hodotopical model of naming processing. Finally, we will consider interaction between language and "amodal" cognitive functions such as working memory and executive control.

2. Investigating the LRM model with DES

In this paragraph, we will discuss how intraoperative DES can contribute to the identification of the language subcomponents involved in a picture naming task. To this intent, we will correlate DES observations with the LRM model (Levelt et al., 1999). Within this framework, the successful achievement of a picture naming task results from a staged process. According to this theory, the timing of the different sub-processes could be estimated from chronometric experiments or from invasive electrophysiological recording (Sahin, Pinker, Cash, Schomer, & Halgren, 2009). Guided by this LRM model, a meta-analysis of fMRI data has been performed (Indefrey & Levelt, 2004), with the aim to infer the anatomical sites of each computational step. However, we have to underline that, although the temporal sequencing of the different subcomponents would suggest serially organized anatomical systems, several sites are activated for each stage, suggesting that each stage is itself performed by a distributed network. In other words, despite a temporal serial model, the spatial underlying architecture appears to be highly non-local (parallel).

Fig. 1 summarizes the correlations between the different types of errors observed when applying DES during a picture naming task and the LRM model, as follows: visual (formal) paraphasia, semantic paraphasia and anomia, morphological verbal paraphasia, phonemic paraphasia, phonetic paraphasia and articulatory disturbances.

First of all, if early visual object recognition is inhibited by DES, it will generate visual paraphasia, for example «cat» instead of «mask». Visual (formal) paraphasia is thus identified by the high degree of visual similarity shared by the target item and the selected one (Mandonnet, Gatignol, & Duffau, 2009).

Semantic paraphasia – for example «sheep» instead of «goat» – corresponds in the LRM model to a wrongly selected lemma. Moreover, within the LRM framework, the lemma selection results from a two steps process: conceptual encoding and lexical selection. For simplicity, we suggest to gather these two stages, by considering these processes as an amodal semantic computation – which in turn can influence the visual recognition by top-down processes (Kherif, Josse, & Price, 2011). Nonetheless, this model cannot explain the double dissociation between picture naming and comprehension, reported by several teams (Bello et al., 2007; Gatignol, Capelle, Le Bihan, & Duffau, 2004). Indeed, by confronting picture naming task and a semantic test of association (Pyramidal and Palm Tree Test, PPTT), DES over the posterior temporal lobe in the left dominant hemisphere elicited selective inability to name the word without comprehension deficit in discrete sites distinct from neighboring cortical areas inducing comprehension disturbances despite naming preservation (but with production of the wrongly selected item on PPTT) (Bello et al., 2007; Gatignol et al.,