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Multi-factorial modulation of hemispheric specialization and plasticity for language in healthy and pathological conditions: A review

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ABSTRACT

This review synthesizes anatomo-functional variability of language hemispheric representation and specialization (hemispheric specialization for language, HSL) as well as its modulation by several variables (demographic, anatomical, developmental, genetic, clinical, and psycholinguistic) in physiological and pathological conditions. The left hemisphere (LH) dominance for language, observed in approximately 90% of healthy individuals and in 70% of patients, is grounded by intra-hemispheric connections mediated by associative bundles such as the *arcuate fasciculus* and inter-hemispheric transcallosal connections mediated by the *corpus callosum* that connects homotopic regions of the left and right hemispheres (RH). In typical brains, inter-hemispheric inhibition, exerted from the LH to the RH, permits the LH to maintain language dominance. In pathological conditions, inter- and intra-hemispheric inhibition is decreased, inducing modifications on the degree of HSL and of language networks. HSL evaluation is classically performed in clinical practice with the Wada test and electro-cortical stimulation, *gold standard* methods. The advent of functional neuroimaging has allowed a more detailed assessment of the language networks and their lateralization, consistent with the results provided by the *gold standard* methods. In the first part, we describe anatomo-functional support for HSL in healthy conditions, its developmental course, its relationship with cognitive skills, and the various modulatory factors acting on HSL. The second section is devoted to the assessment of HSL in patients with focal and drug-resistant epilepsy (FDRE). FDRE is considered a neurological model associated with patterns of language plasticity, both before and after surgery: FDRE

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patients show significant modification of language networks induced by changes mediated by transcallosal connections (explaining inter-hemispheric patterns of language reorganization) or collateral connections (explaining intra-hemispheric patterns of language reorganization). Finally, we propose several predictive and explicative models of language organization and reorganization.

1. Introduction

This present review focuses on two main concepts of language neuroscience: language variability and language plasticity assessed in healthy volunteers and in patients with cerebral lesions, and specifically patients with focal and drug-resistant epilepsy (FDRE). Two major characteristics of language reorganization are targeted, including the hemispheric specialization for language (HSL) and the cerebral representation of specialized language regions (intra-hemispheric language mapping, LM). The aim of this paper is to review the features of these two concepts (variability and plasticity) and two major characteristics (HSL and LM) and reveal how they are modulated by various variables (demographic, clinical, anatomical, psycholinguistics). The dominance of language in a given hemisphere was first conceptualized as HSL by Marc Dax and his son (Manning & Thomas-Anterion, 2011). Broca himself previously associated the occurrence of aphasia after a lesion of the left hemisphere (LH) with the high prevalence of right-handedness in humans, suggesting that left-handers would be aphasic after a right hemisphere (RH) lesion, which, as we will see, is not the case (Broca, 1876). During this period, the occurrence of a hemisphere, particularly the LH, controlling both the right hand and language was considered the "dominant" or "major" hemisphere, whereas the RH was considered the "minor" hemisphere. Later neuropsychological studies and the pre-surgical Wada procedure, which tests language functions after anesthesia is administered to only one hemisphere (Wada & Rasmussen, 1960), confirmed that a lesion of the LH leads to aphasia and apraxia in most individuals. A major finding regarding the role of the hemispheres in language functions came from investigations of patients who had undergone surgical section of the corpus callosum. These investigations revealed the existence of "two brains," with the left brain hosting linguistic functions, such as phonology and syntax, and the right brain involved in paralinguistic functions, such as emotional and context processing. These reports on split-brain patients noted the crucial role of inter-hemispheric callosal connectivity in establishing the specialization of each hemisphere (review in Gazzaniga, 2000).

The advent of functional imaging was a turning point in research on HSL because it enabled the measurement of asymmetries in activation at the hemispheric and/or regional levels during various language tasks. Because the Wada procedure is performed by testing language functions after anesthetizing each hemisphere separately, the first method that was used to classify individuals in terms of their dominant hemisphere from neuroimaging involved calculating the difference in activation between the hemispheres by subtracting the right side activation from the left side activation, and this subtraction method is still commonly used. It is remarkable that the search for the underpinnings of anatomical and functional specificity of the hemispheres for language had mainly relied on this very simple model (left minus right) at the hemispheric and regional levels. This asymmetry index is efficient because it allows for the investigation of an elementary network composed of pairs of areas located in mirrored locations and linked by callosal connections that underpin inter-hemispheric interactions. A first step has been to demonstrate the validity of fMRI for the assessment of HSL by showing consistent results between fMRI and the gold standard methods (Adcock, Wise, Oxbury, Oxbury, & Matthews, 2003; Baciu, Juphard, Cousin, & Bas, 2005; Baciu et al., 2001, 2003; Binder et al., 1996; Carpentier et al., 2001; Rutten, Ramsey, van Rijen, & van Veelen, 2002; Sabsevitz et al., 2003; Swanson, Sabsevitz, Hammeke, & Binder, 2007; Woermann et al., 2003). In summary, regardless of the technology (fCTD, fMRI) or methodology (hemispheric, regional) that is applied to the compute such an index, the resulting indices show a high consistency (for a review see Dym, Burns, Freeman, & Lipton, 2011). In particular, atypical representations, such as rightward language lateralization or dissociative patterns of dominance between language production (frontal regions) and language perception (temporal regions), were validated by fMRI after being detected by the gold standard methods (Baciu et al., 2003; Backes et al., 2005; Thivard et al., 2005). Neuroimaging uncovered that atypical dominance for language exists in healthy participants and thus opened the way for investigation of inter-individual variability in the neural organization f language, as well as individual factors associated with such variability, with the aim of understanding the rules that govern the establishment of the HSL. Although under specific conditions the hemispheric (or regional) asymmetry index measured with neuroimaging is equivalent to Wada testing (Binder, 2011) and thereby to HSL, one should emphasize that any asymmetry measure performed during any language task is not equivalent to a measure of hemispheric dominance. Only a few language tasks have been validated as adequately capturing an individual's HSL classification, and these do not allow fine-grained linguistic analysis (Dym et al., 2011). One should indeed keep in mind that, as it will be further developed, the identification of essential language areas can only be validated using invasive methods in pathological states, which underlines the critical contribution of research on epileptic patients.