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Review

A two-level model of interindividual anatomo-functional variability of the brain and its implications for neurosurgery

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ABSTRACT

The classical dogma of localizationism implicitly resulted in the principle of a similar brain functional anatomy between individuals, as for example the pars opercularis of the left "dominant" hemisphere corresponding to the speech area. This fixed "single brain" model led neurosurgeons to define a set of "eloquent" areas, for which injury would induce severe and persistent neurological worsening, making their surgical resections impossible. Therefore, numerous patients with a cerebral lesion justifying surgery were *a priori* not selected for resection and lost a chance to be treated. In fact, advances in brain mapping showed a considerable inter-individual variability explained by a networking organization of the brain, in which one function is not underpinned by one specific region, but by interactions between dynamic large-scale delocalized sub-circuits. Indeed, using non-invasive neuroimaging, a variability of both structural and functional anatomy was demonstrated in healthy volunteers. Moreover, intraoperative electrical stimulation mapping of cortex and white matter tracts in awake patients who underwent surgery for tumor or epilepsy also showed an important anatomo-functional variability. However, a remarkable observation is that this variability is huge at the cortical level, while it is very low at the subcortical level. Based upon these intrasurgical findings, the goal of this review is to propose a two-level model of inter-individual variability (high cortical variation, low subcortical variation), breaking with the traditional rigid workframe, and making neurosurgery in traditionally presumed "eloquent" areas feasible without permanent deficits, on condition nonetheless to preserve the "invariant common core" of the brain.

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1. Introduction

Although interactions between cognitive neurosciences and neurosurgery are usually fruitful, they may nonetheless be also harmful. Indeed, the classical dogma of localizationism implicitly resulted in the principle of a similar brain functional anatomy between individuals. For example, according to this view, the pars opercularis of the left "dominant" hemisphere corresponds to the speech area, and the posterior part of the left superior temporal gyrus corresponds to the verbal comprehension area. In clinical practice, this fixed cognitive model of a "single brain" led neurosurgeons to define a simplistic set of so-called "eloquent" areas (Sawaya et al., 1998), for which any injury would irremediably induce severe neurological worsening (as Broca's area, Wenicke's area or Rolandic area), making their surgical resections impossible. Therefore, numerous patients with a cerebral tumor or intractable epilepsy that justified surgery, were *a priori* not selected for resection and lost a chance to be treated, illustrating the possible negative impact of erroneous models of cognitive neuropsychology on neurosurgery.

Surprisingly, despite the fact that the overwhelming statistical support for the classical position of cerebral functions has been challenged in the past century, with rare exceptions, individual anatomic variations in the brain have nonetheless received few attention. Yet, in a review of the literature published in 1975, Whitaker and Selnes already wrote that "the conclusion seems inescapable that each person's brain may be as individual as his physiognomy. This conclusion should come as no surprise if one extrapolates from the large number of animal studies which suggests that the biochemical and morphological structure of the brain is modified by experience, since clearly, no two individuals share and identical set of experiences" (Whitaker & Selnes, 1976). However, it is worth noting that only anatomic variations in the cortex have been reported.

Here, the goal of this review is to highlight the concept of inter-individual anatomo-functional variability of the central nervous system (CNS) in surgical selection and planning. Indeed, in the modern literature, owing to the development of non-invasive neuroimaging techniques, a large amount of data has confirmed the existence of variations in both structural and functional anatomy between individuals (in healthy volunteers as well as in patients). This is possible only in a dynamic and networking framework of brain processing, breaking with the traditional and rigid single brain model. From a clinical perspective, such connectomal account of the CNS organization opens the door to massive surgical resections in areas classically considered "critical", without generating permanent deficits, thanks to the use of intraoperative stimulation mapping in awake patients (De Benedictis & Duffau, 2011; Duffau, 2014a). However, a remarkable observation is that, although intrasurgical electrical mapping has evidenced a huge inter-individual variability at the cortical level, it also showed that brain variations were minimal at the subcortical level.

Clearly, the present article is not an extensive review on anatomo-functional variability, but a review mainly based upon the own authors' work on intraoperative electrical mapping of both cortex and subcortical white matter tracts—even though similar ideas, proposals and works exist elsewhere, as partly discussed below. After this overview of structural and functional variability of the brain, with special emphasis on the data provided by direct electro-stimulation, the second aim is to propose a two-level model of inter-individual variability (high cortical variability, low subcortical variability), by highlighting the concept of an "invariant common core" of the brain. Beyond its fundamental interest in neurosciences, the implications of this original model in neurosurgery are also discussed.

2. Variability of brain structural and functional anatomy in normal individuals

2.1. *Structural variability*

It is currently well-known that the anatomy of the brain is highly variable across individuals, especially at the cortical level (Le Goualher et al., 1999; Thompson, Schwartz, Lin, Khan, & Toga, 1996). Ono et al. have reported a morphological atlas to classify the myriad sulcal patterns that exist upon the cortical surface (Ono, Kubik, & Abernathey, 1990). Remarkably, regions of higher anatomical variability revealed using recent automated methods were generally similar to those identified manually by Ono et al (Ono et al., 1990), namely in some frontal areas and temporoparietal areas (Kang, Herron, Cate, Yund, & Woods, 2012). Indeed, a considerable variability in gross anatomy of the perisylvian gyri has extensively been described (Rubens, Mahowald, & Hutton, 1976). For example, Heschl's gyrus, a part of the superior temporal plane, exhibits a highly variable morphology that includes one to three gyri per hemisphere, with the number of gyri varying between hemispheres (Marie et al., 2015; Smits et al., 2011). In the same vein, it has been observed a morphological variability of human occipital sulci, related to inter-individual and inter-hemispheric differences in their presence, origin, type, segmentation, intersection and length (Iara & Petrides, 2007; Malikovic et al., 2012). Furthermore, by combining neuroimaging-confirmed and anatomical topographic characteristics of the inferior precentral sulcus, that borders the classical "Broca's area", Ebeling et al. grouped frontal opercula into four different general patterns of sulcus formation: although most frequently, the inferior precentral sulcus was the sulcus posterior to the anterior ascending sylvian ramus (95% in the MR study, 87% in the anatomic study), an additional sulcus was occasionally interposed (5%, 10%), or an ascending ramus was absent (0%, 3%) (Ebeling, Steinmetz, Huang, & Kahn, 1989).

A "sulcal root" model that relies on gyri buried in the depth of the sulci has been proposed to explain this morphometric variability (Régis et al., 2005). According to this hypothesis, anatomic variability at the adult stage is thought to result from the chaotic behavior of the folding process (Thom, 1975). There is also evidence for a major genetic component (Thompson et al., 2001). Moreover, structural changes of the gray matter can occur in adults, these modifications being able to be induced by training (Draganski et al., 2004).