We had the opportunity to review the study entitled: “Iterative surgical resections of diffuse glioma with awake mapping: How to deal with cortical plasticity and connectomal constraints?”1 This study has some limitations if we observe it under the perspective of current neurooncology “mainstream” focused on biomolecular profile of tumors and the choice of the best adjuvant treatment. Indeed, here there is no molecular analysis, no tumor subtype characterization, not an outstanding number of patients were recruited, no randomization. Nonetheless, this study is a definitive milestone. It represents, indeed, a further step in the groundbreaking theory of mind that has recently moved our interpretation of brain functioning from a classical “localizationist” view into a “hodotopical” framework.2-4

According to this increasingly recognized view, the distinction between eloquent and rigidly specialized as opposed to not-eloquent brain areas is insufficient to explain the complexity of brain processing, especially for higher cognitive functions. More realistically, multiple brain areas are simultaneously involved in generating complex behaviors and it is also possible that each region has characteristics of pluripotency. In the light of a cortex organized into networks with multimodal properties, the concept of “specialized” centers should be more realistically replaced by “functional” epicenters. What we still need to understand is the distribution and the spatial and temporal hierarchy of each node of the network to gain precise information applicable in the operating room.

The second point in this new vision of brain functioning concerns neuroplasticity and its potential.5,7 Cerebral plasticity is a permanent neural and synaptic processing occurring in the short- and long-term, aimed to adapt networks of the brain during ontogenetic development and learning as well as after lesions involving the central nervous system. Several hypotheses about the physiological mechanisms underlying plasticity have been provided. At a microscopic scale, these mechanisms seem to be essentially represented by modulations of synaptic efficiency, activation of latent connections, impulse synchrony changes, and ultimately neurogenesis. At a macroscopic scale, functional redundancies, cross-modal plasticity with sensory substitution, and even large-scale morphological changes are supposed to be involved. This study has the huge merit of demonstrating the truth about neural plasticity, its potential, and its relevance in brain tumor surgery. Above all, this study well describes the limits of this process. Thus, as brilliantly stated by the authors, surgical resection in eloquent areas is feasible without generating permanent deficits thanks to such neural plasticity and network reshaping, on the condition to preserve an “invariant common core” of the brain, composed of noncompensable input and output cortical areas and mainly by white matter tracts, which represent the ultimate connectomal constraints of neuroplasticity.7

According to these results, through a deep knowledge of brain connectivity (intra and interhemispheric), we could predict resectability, postoperative deficit, and eventually oncological outcome on an individual basis. In practice, a dynamic strategy to the surgical treatment of brain tumors can be envisaged and this study demonstrates that this is possible in the clinical setting.

Furthermore, we can suppose that a similar switch from a static use of preoperative functional imaging to an aware use of neuroimaging and biomathematical models to examine brain functional interactions and connectivity is realistic.

Does this mean that we can predict, before surgery, the potential and the patterns of postsurgical remapping? There are clues that this is possible.8,9 Furthermore, it is already conceivable that methods to induce and guide brain plasticity through electrical stimulation, TMS, functional rehabilitation, and
pharmacological interventions can be developed to promote connectivity. These techniques can be used not only to promote postsurgical recovery, but also for a preoperative strategy aimed to re-map, or at least explore the potential for remapping, the functional brain circuits in order to allow a greater extent of resection while avoiding postsurgical deficits. We welcome this study and the deep understanding of the interactions of brain and tumors of their authors.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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