Deep brain stimulation for schizophrenia

TO THE EDITOR: We read with great interest the review by Mikell et al.3 (Mikell CB, Sinha S, Sheth SA: Neurosurgery for schizophrenia: an update on pathophysiology and a novel therapeutic target. J Neurosurg 124:917–928, April 2016). These authors summarize current understanding of the pathophysiology of schizophrenia based on dysfunction in dopaminergic and glutamatergic signaling. They suggest several nodes of the basal ganglia–thalamocortical circuit as therapeutic targets for deep brain stimulation (DBS): the hippocampus, the ventral striatum, and the associative striatum.3 Regarding this dopamine dysregulation–based hypothesis, we believe that there are other targets that could be useful for DBS: the mediodorsal thalamus and the internal globus pallidus.1,4,5,9 Moreover, in the last few years, findings from voxel-based morphometry, diffusion tensor imaging, and functional MRI suggest structure and functional alterations of the medial prefrontal cortex, specifically the area correlated to the anterior midline node of the default mode network.6,8 This area corresponds to the subcallosal cingulate gyrus, which includes Brodmann area 25. The failure of task-related deactivation in this medial frontal cortex is related to the symptoms of schizophrenia. Actually, a meta-analysis of the whole-brain voxel-based approach revealed that abnormalities in white matter areas in schizophrenia were consistently identified across the studies in only 2 locations, one of them corresponding to this anterior cingulate subgenual area.2 This region has been stimulated with DBS in other neuropsychiatric disorders, and in our experience in treatment-resistant depression, no associated complications have been observed.7 We suggest that this could be another possible target for the treatment of resistant schizophrenia.

Schizophrenia remains one of the leading causes of disability worldwide, with 30% of patients refractory to treatment. We agree that given the severity of this disease and its high consumption of resources, new treatment strategies are needed. We are conducting a prospective, randomized, double-blind clinical trial (clinical trial no.: NCT02377505, clinicaltrials.gov) aimed at assessing the tolerability and efficacy of DBS in refractory schizophrenia (founding Grant Nos. PI12/00042 [E.A.] and PI12/00686 [S.S.] from the Instituto de Salud Carlos III).

We randomized the therapeutic target (nucleus accumbens vs subgenual area), and after the start of stimulation and a period of clinical stability, we made a crossover phase of generator on or off. We are studying treatment response in terms of neuroimaging (MRI, PET) and clinical variables. Completion of this ongoing study and an exhaustive analysis of the data are needed for definitive answers.

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Failed microvascular decompression surgery

TO THE EDITOR: I read the article by Bigder and Kaufmann with great interest (Bigder MG, Kaufmann AM: Failed microvascular decompression surgery for hemifacial spasm due to persistent neurovascular compression: an analysis of reoperations. J Neurosurg 124:90–95, January 2016). I would like to address several comments to the authors. In the article, the authors mentioned that microvascular decompression (MVD) is no guarantee of a hemifacial spasm (HFS) cure, presumably given a failure rate of nearly 10%. Despite all our efforts, we do know that there is a discrepancy between technical and clinical success in the operation; that is, the surgeons are quite sure of decompression during the surgery, but the clinical results do not always correspond. In this respect I agree with the authors. However, I do wonder what rate of failure would fulfill the authors’ guarantee of success because I believe that our mission continues to be improvement of the surgery as long as MVD is the only curative treatment for HFS.

Previously, in a report on patients with trigeminal neuralgia in whom treatment had failed, Jannetta and Bissonnette described, “a ‘failed’ patient is a signal that we are not perfect and that the forces of nature have again outwitted us. We cannot hide these failures, avoid them, or ignore them. Rather, we can learn from them and, frequently, can make the patients feel better or even cure them.” The article by Bigder and Kaufmann illustrates 3 important points that can help us achieve better outcomes. Firstly, exposure of the sigmoid sinus and inferior floor of the cerebellum should never be skipped. Secondly, the vertebral artery should be properly transposed but not interposed. Thirdly, we should try our best to mobilize the responsible artery in the presence of perforating arteries. I fully agree with their conclusion that caudal side exposure is very important for observation of the entire facial nerve as well as the protection of hearing function. In addition, I mobilize the arterial loops close to the facial root exit zone (fREZ) that represent potential causes of HFS in the future to avoid new neurovascular compression, if this maneuver can be achieved safely. I believe that correct application of all these procedures in the initial surgery will increase the rate of success.

Finally, I would like to discuss the importance of preoperative imaging, which the authors did not mention in their article. The techniques of preoperative MRI are well advanced and established. However, I am afraid that neurosurgeons may depend on MRI too much. Vascular components can be located nearby or even conflict with the seventh and eighth cranial nerve complex in the absence of symptoms and can represent the cisternal part that is not responsible for the symptoms in patients with HFS. Consequently, the proximal part of the fREZ may be overlooked.

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References