Posteromedial Hypothalamic Deep Brain Stimulation for Refractory Aggressiveness

In carefully selected patients, DBS of the posteromedial hypothalamus can be considered an effective procedure for the treatment of refractory trigeminal autonomic cephalalgias, aggressive behavior, and MS-related trigeminal neuralgia in the first trigeminal branch. Only larger and prospective studies along with multidisciplinary approaches (including, by necessity, neuroimaging studies) can lead us to better patient selection that would reduce the rate of nonresponders ¹⁾

Chronic high frequency stimulation (HFS) of the posteromedial hypothalamus (PMH) has been the first direct therapeutic application of functional neuroimaging data in a restorative reversible procedure for the treatment of an otherwise refractory neurological condition; in fact, the target coordinates for the stereotactic implantation of the electrodes have been provided by positron emission tomography (PET) studies, which were performed during cluster headache attacks. HFS of PMH produced a significant and marked reduction of pain attacks in patients with chronic cluster headache (CCH) and in one patient with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). The episodes of violent behaviour and psychomotor agitation during the attacks of CCH supported the idea that the posteromedial hypothalamus could be also involved in the control of aggressiveness; this has been previously suggested, in the seventies, by the results obtained in Sano's hypothalamotomies for the treatment of abnormal aggression and disruptive behaviour. On the basis of these considerations, Franzini et al. performed HFS of the PMH and controlled successfully violent and disruptive behaviour in patients refractory to the conventional sedative drugs. Finally, they also tested the same procedure in three patients with refractory atypical facial pain, but unfortunately, they did not respond to this treatment ²¹.

Case series

Data were collected retrospectively from nine patients, who received bilateral stereotactic pHyp-DBS for the treatment of medically intractable aggressive behavior, focusing on five patients who also had DRE. All patients were treated at the Colombian Center and Foundation of Epilepsy and Neurological Diseases-FIRE (Chapter of the International Bureau for Epilepsy), in Cartagena de Indias, Colombia from 2010 to 2014. Each case was evaluated previously by the institutional ethical committee, assessing the impact of aggressive behavior on the patient's family and social life, the humanitarian aspects of preserving the safety and physical integrity of caregivers, and the need to prevent self-harm. Epilepsy improvement was measured by a monthly seizure reduction percentage, comparing preoperative state and outcome. Additional response to epilepsy was defined by reduction of the antiepileptic drugs (AEDs). Aggressive behavior response was measured using the Overt Aggression Scale (OAS).

Results: All the patients with DRE associated with IAB presented a significant decrease of the rate of epileptic seizures after up to 4 years follow-up, achieving a general 89.6% average seizure reduction from the state before the surgery. Aggressiveness was significantly controlled, with evident improvement in the OAS, enhancing the quality of life of patients and families.

Significance: In well-selected patients, DBS of the pHyp seems to be a safe and effective procedure for treatment of DRE associated with refractory aggressive behavior. Larger and prospective series are needed to define the pHyp as a target for DRE in different contexts ³.

Medical records of 6 patients treated with PMH DBS for intractable aggressiveness were reviewed. The therapeutic effect on behavior was assessed by the Inventory for Client and Agency Planning preoperatively and at the last follow-up visit.

Results: Two patients died during the follow-up period due to causes unrelated to the neurosurgical treatment. Five of 6 patients experienced a significant reduction in aggressiveness (the mean Inventory for Client and Agency Planning general aggressiveness score was -47 at baseline and -25 at the last follow-up; mean follow-up 3.5 years). Similar responses were obtained with low- and high-frequency stimulation. In 4 cases, the patients' sleep patterns became more regular, and in 1 case, binge eating and polydipsia ceased. One of the 3 patients who had epilepsy noticed a 30% reduction in seizure frequency. Another patient experienced a marked sympathetic response with high-frequency stimulation during the first stimulation trial, but this subsided when stimulation was set at low frequency. A worsening of a previous headache was noted by 1 patient. There were no other side effects.

Conclusions: In this case series, 5 of 6 patients with pathological aggressiveness had a reduction of their outbursts of violence after PMH DBS, without significant adverse effects. Prospective controlled studies with a larger number of patients are needed to confirm these results ⁴.

Case reports

A 26-yr-old man diagnosed with WS presenting with uncontrollable self and heteroaggressiveness and disruptive behavior refractory to pharmacological treatment and under severe physical and mechanical restraining measures. The patient was successfully treated with bilateral PMH DBS resulting in affective improvement, greater tolerance for signs of affection, regularization in his sleep pattern and appetite disturbances at 12-mo follow-up. A detailed description and video of the procedure are presented, and a review of the clinical characteristics of WS and the utility and benefits of PMH DBS for refractory aggressiveness are reviewed.

Conclusion: To our knowledge, this is the first case of refractory aggressiveness described in WS as well as the first patient with WS successfully treated with PMH DBS $^{5)}$

a case of deep brain stimulation in a patient with severe aggression refractory to conservative treatment. The targets of the stimulation were set bilaterally in the posteromedial hypothalamus and - in a second procedure due to its ineffectiveness - in the nucleus accumbens (NAcc) bilaterally.

Methods: In the first stage, we implanted electrodes into the posteromedial hypothalamus, after obtaining consent of the Bioethics Committee. In the early postoperative period, we observed significant improvement in the range of 50-90% in terms of quantity and quality of the attacks of aggression. After about 3 weeks, attacks of aggression started to return. Despite changes in the stimulation parameters there was no improvement. For this reason, based on the experience of

surgery in patients with obsessive-compulsive disorder, Tourette syndrome and with morbid obesity, we decided to implant electrodes into the NAcc.

Results: After 15 months of follow-up, the patient has no aggressive behavior, with no side effects.

Conclusions: Although the stimulation of the posterior-medial hypothalamus did not bring long-term benefits, its combination with bilateral stimulation of the NAcc practically freed the patient from aggressive disorders. It significantly improved the patient's quality of life ⁶⁾.

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