

Commentary: Amygdala and Hypothalamus: Historical Overview With a Focus on Aggression

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Part of the content of this manuscript has been presented at the plenary session of the following meetings: 1. 17th Quadrennial Meeting of the World Society for Stereotactic and Functional Neurosurgery - WSSFN (Berlin, Germany; June 26-29, 2017; sponsored by the WSSFN); 2. V Congress of the Spanish Society for Stereotactic and Functional Neurosurgery - SENFE (Palma de Mallorca, Spain; Sept 27-29, 2017; sponsored by the SENFE); 3. III International Conference on Functional Neurosurgery: The Past, the Present, and the Future (Moscow, Russia; May 11-12, 2017; sponsored by the Russian Society of Functional Neurosurgeons - RAFN); and 4. XIII Brazilian Congress of Stereotactic and Functional Neurosurgery (Gramado, Brazil; May 24-26, 2018; sponsored by the Brazilian Society for Stereotactic and Functional Neurosurgery - SBENF).

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Received, November 20, 2018.

Accepted, January 31, 2019.

Published Online, March 13, 2019.

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Congress of Neurological Surgeons

Different from other psychiatric disorders, impulsive aggression is not a disease but rather a symptom of many psychiatric disorders, including schizophrenia, severe/profound mental retardation, autism, bipolar mood disorder, and post-traumatic stress disorder, among others. In fact it is highly prevalent and a major health problem. When refractory to the best conservative management, surgery may be an option.

The authors have done a great job reviewing a vast literature regarding the role of the amygdala and of the hypothalamus or their surgical manipulation (ablation or DBS) on aggressiveness.¹ Numerous studies were reviewed.¹ Unluckily, the majority of them were from the 1960s and 1970s, consisting of open-label trials and using subjective measures of behavior, resulting in a low level of evidence, so preventing to make any formal treatment recommendation. It is unfortunate that such a volume of information is essentially useless under the rigid scientific standpoint. One should learn from history. It is never redundant to stress the importance of the use of “objective” tools to evaluate symptom severity, functioning and quality of life and to establish clear-cut inclusion and exclusion criteria.

All these studies present a high risk of bias since none is a clinical trial. A randomized clinical trial similar to that performed by Lopes et al² in OCD patients (gamma ventral capsulotomy) would be highly desirable. Non-invasive techniques, such as MR-guided focused ultrasound or gamma-knife to perform lesion/sham-lesion, could be used to this end.

In our experience, the majority of the patients with impulsive aggression undergoing surgery are very severely impaired. One would expect a greater risk of DBS complications in this particular group of patients, especially in those with self-aggression, such as infection, skin erosion, and lead fracture/disconnection. For this reason, we tend to favor ablative surgery for this group of patients.

One should keep in mind that, besides amygdalotomy, posteromedial hypothalamotomy, and hypothalamus DBS, other

procedures, in isolation or association, have been reported as successful in the treatment of impulsive aggression, such as anterior cingulotomy, subcaudate tractotomy, limbic leucotomy (anterior cingulotomy + subcaudate tractotomy), anterior capsulotomy, and more recently, nucleus accumbens DBS.

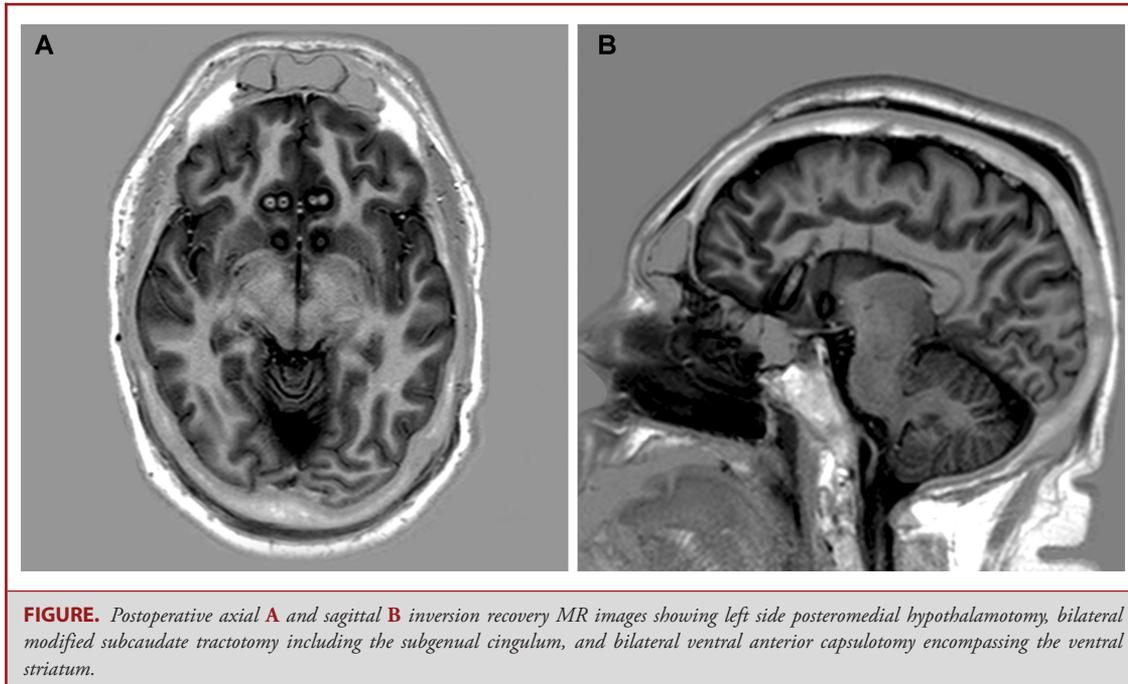
In our center, impulsive aggression is undoubtedly the most common psychiatric problem referred for surgery, and schizophrenia, severe/profound mental retardation, and autism are the psychiatric disorders most commonly presenting with refractory aggressiveness.

Among the psychiatric conditions requiring surgery, aggressiveness, in our hands, is the one that poses the greatest difficulty. For this reason, along the last 20 yr or so, we have changed our approach a few times in an attempt to achieve a better control of this symptom.

When we started operating for impulsive aggression, we elected bilateral amygdalotomy as the procedure of choice. The rates of failure and recurrence were high, though.

In 2001, we proposed the use of functional neuroimaging studies to determine the best target to treat varied psychiatric disorders.³ Using this tool, we observed hypermetabolism in the anterior cingulate gyrus of our patients who failed to respond to amygdalotomy, which led us to consider bilateral anterior cingulotomy in these patients in a second procedure. Da Costa⁴ had already reported this combination of targets (bilateral amygdalotomy + bilateral anterior cingulotomy).

Although the results showed improvements, the number of failures was still significant. Once more taking advantage of functional neuroimaging studies, hypermetabolism of the orbitofrontal and/or prefrontal dorsolateral cortex was detected in these patients. Based on these results and on the report of Cox and Brown, 1977,⁵ we performed bilateral subcaudate tractotomy in those patients who failed to respond to bilateral amygdalotomy + bilateral anterior cingulotomy. The results improved even more, although the number of failures remained considerable.



By this time, we suspected that one of the targets we had been using was inadequate and responsible for our failures. Since the use of anterior cingulotomy and subcaudate tractotomy was supported by functional neuroimaging findings, we decided to replace bilateral amygdalotomy with unilateral posteromedial hypothalamotomy, on the dominant hemisphere (less risky than when performed bilaterally). Again, the results improved with this strategy.

Although much rarer, failures still happened. In such cases, following the lead of other authors,⁶⁻⁹ we added bilateral ventral anterior capsule (encompassing the ventral striatum) to our previous procedure (dominant side posteromedial hypothalamotomy + bilateral anterior cingulotomy + bilateral subcaudate tractotomy), achieving control of aggressiveness in practically all cases.

But then we were using too many targets, and still had ahead of us the difficult task of trying to reduce their number while maintaining the significant control of aggressiveness achieved after so much struggle. The way we devised to do that was by using a technique we first described in 2012, the modified subcaudate tractotomy: by merely changing the anteroposterior coordinate of the target, we could include the subgenual cingulum in the subcaudate tractotomy lesion, making it theoretically possible to eliminate the anterior cingulotomy from our surgical strategy.¹⁰ So far, we have employed this new combination of targets (dominant side posteromedial hypothalamotomy + bilateral modified subcaudate tractotomy + bilateral ventral anterior capsulotomy encompassing the ventral striatum) in 4 patients, obtaining complete resolution of impulsive aggression in all (Figure). We are currently starting a 2-center prospective study

to evaluate the effectiveness of this new approach in 15 consecutive aggressive patients (schizophrenia, n = 5; autism, n = 5; and severe/profound mental retard, n = 5) refractory to the best conservative management.

Disclosure

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

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Acknowledgments

The author would like to express his gratitude to the colleagues Paulo C. Ragazzo, MD, PhD, Paulo M. Oliveira, MD, MSc, Manoel D. Reis, MD, and Telma M. Campos, BSc, for their careful evaluation and valuable comments on patients undergoing surgery for psychiatric disorders at the Goiânia Neurological Institute.