

# Stereotactic Ablative Surgery in Autism: A Cocktail of Lesioned Brain Targets?

Marwan Hariz<sup>a, b</sup>

<sup>a</sup>Department of Clinical Neuroscience, Umeå University, Umeå, Sweden; <sup>b</sup>UCL Institute of Neurology, London, UK

Dear Editor,

I read the paper of Torres et al. [1] about surgery for autism with great interest. I was wondering how so many important issues could have been missed both by the authors and by the Reviewers. With this letter, I hope that the authors will be given the opportunity to provide a reply including necessary clarifications to their published work.

Please let me state from outset: I am all for trying pertinent surgical treatments on desolate patients whose suffering is very therapy-refractory, and whose quality of life, and indeed life, is so seriously compromised. However, some sort of rationale needs to be provided to a surgical intervention on such patients, especially in a scientific clinical report, so peers can learn and maybe emulate with good conscience the procedures described by the authors, in potential surgery on similar patients. The authors report a “retrospective study, approved by the Local Ethics Committee,” in which they selected all the Autism Spectrum Disorder (ASD) patients, treated for serious and refractory aggressiveness and obsessive-compulsive disorder at their institution, with a follow-up of at least 2 years.

Among “the Inclusion Criteria,” they list: “Diagnosis of ASD, with severe drug-resistant aggressiveness and obsessive behaviours, by at least 2 separate independent psychiatrists/neurologists, and for at least 5 years.” In Table 1, in the column “Autism diagnosis year,” none of the

patients had a diagnosis of at least 5 years (their diagnosis ranged between zero and 4 years). Also in Table 1, under the column “Observations,” the authors provide a description of the symptoms that the patients suffered from, however, no symptoms are given for patients #3 and #5. Finally, in same table, no follow-up duration is provided for patient #5.

Concerning the capsulotomies, the authors wrote: “The coordinates for the capsulotomies were  $x$ -19–21 mm bilateral to midline,  $y$ -0, and  $z$ -0, which corresponds approximately to the middle area of the capsules at the level of the posterior region of the putamen.” No matter how I consider this, I can make no sense of these coordinates: coordinate  $y$ -0 in relation to what? To midcommissural point? To anterior commissure? If it is the latter, as I suspect, then how can this coordinate be “at the level of the posterior region of the putamen”?

The flow chart shown in Figure 1 explaining the selection protocol leading to surgery discloses the following surgical procedures: “Surgery: amygdalotomy plus bilateral capsulotomy.” Yet, as shown in the paper and discussed below, patients were submitted to several other procedures on other brain targets not listed in the flow chart.

In the paragraph on “Preoperative Evaluation,” it is stated “All patients underwent an MRI with DTI to assess their baseline connectivity.” Yet, the length of follow-up, as shown in Table 1, extends from 6 years in patient #10

to 26.5 years in patient #1, including patient #3 with 20 years and patient #9 with 19 years follow-up. Was the DTI technology mature enough 20 or 26 years ago to enable assessment of baseline connectivity?

According to Table 1, most patients underwent several subsequent procedures as follow:

Patient #1: “bilateral capsulotomy and left estria terminalis Lesion” then “capsulotomy enlargement,” then “right estria terminalis and left amygdalae.”

Patient #2: “bilateral capsulotomy, left estria terminalis, and right amygdalotomy,” then “right estria terminalis, left amygdalotomy, and bilateral cingulum.”

Patient #3: “left estria terminalis and left cingulum,” then “right estria terminalis, bilateral capsulotomy, and bilateral cingulotomy.”

Patient #4: “bilateral capsulotomy and left amygdalae.”

Patient #5: “bilateral anterior capsulotomy, right cingulotomy, and left amygdalotomy,” then “GK radiosurgery, right capsulotomy, and left cingulotomy and left amygdalotomy.”

Patient #6: “Left estria terminalis and bilateral capsulotomy,” then “left amygdala and right cingulum.”

Patient #7: “Bilateral capsulotomy, left estria terminalis, and right Amygdala.”

Patient #8: “bilateral capsulotomy. Left amygdalotomy,” then “GK radiosurgery: Right amygdalotomy and left Cingulotomy.”

Patient #9: “Bilateral capsulotomy, left estria terminalis, left cingulum, right amygdalotomy,” then “Right amygdalotomy enlargement, right cingulotomy,” then “left capsula, bilateral cingulum, left amygdala, right estria terminalis.”

Patient #10: “Bilateral capsulotomy, right amygdalotomy, and left cingulotomy,” then “GK radiosurgery left cingulum, and left amygdala.”

With respect to the multitude of ablated brain targets shown above, the authors wrote that patients had serial follow-ups after surgery and “According to the patient’s clinical situation, a second and/or third operation or GK procedure was offered,” and “In all cases, radiofrequency or irradiation was applied to the stria terminalis, amygdala, and unilateral cingulum.” One may wonder what exactly was the rationale for choosing this or that or those target(s), then again this or that or those other target(s) on left or right side, at each occasion?

Concerning the size of the lesions, that the multicolour Figure 4 is said to illustrate, the authors provide the mean volume of the various lesions: for capsulotomies the mean lesion volume was “1.73 mm<sup>3</sup>,” for cingulotomy “2.47 mm<sup>3</sup>,” for amygdalotomy “1.26 mm<sup>3</sup>,” and for stria ter-

minalis lesion “6.77 mm<sup>3</sup>.” Assuming a stereotactic lesion is a spheroid the volume of which can be calculated by the formula  $\frac{4}{3}\pi r^3$ , and then the mean diameter of the lesion would be 1.48 mm for capsulotomy, 1.66 mm for cingulotomy, 1.34 mm for amygdalotomy, and 2.34 mm for stria terminalis lesion. In my humble opinion, the provided volumes of the various stereotactic lesions simply do not make sense.

In summary, I agree with the authors that the described patients “are extremely severe and are usually condemned to live under mechanical restraint, which exerts an important effect in their quality of life and life expectancy, so there is no reason to exclude them from beneficial treatments.” However, to be credible and reproducible in other centres, this practice of repetitive lesions on various unilateral or bilateral brain targets should be solidly anchored in a valid rationale and documentation, lest the whole issue of ablative stereotactic neurosurgery for these desolate patients will be jeopardized.

A final reflection: The paper of Torres et al. [1] is published in *Stereotactic and Functional Neurosurgery*. As such it must have been peer-reviewed by true peers who ought to be expert in, and attentive to, this very field. I can guess that the various peer reviewers of this paper may have had comments related to ethical issues surrounding these procedures, but the peer reviewers ought also to have contributed to help the authors to improve their work by pointing out the issues that I highlighted above. Thus, it is my hope that the authors be now given the opportunity to reply and clarify the points that I have raised.

### Conflict of Interest Statement

The author has no conflict of interest to declare.

### Funding Sources

No funding was received.

### Author Contributions

M.H. is the sole author.

### Reference

- 1 Torres CV, Martínez N, Ríos-Lago M, Lara M, Alvarez-Linera J, Cabanyes J, et al. Surgery and radiosurgery in autism: a retrospective study in 10 patients. *Stereotact Funct Neurosurg*. 2021;99(6):474–83.