

Long-term Follow-up Study of MRI Guided Bilateral Anterior Capsulotomy in Patients with Refractory Anorexia Nervosa - Comments for publication

Ludvic Zrinzo MD PhD FRCS

Unit of Functional Neurosurgery

Sobell Department of Motor Neuroscience and Movement Disorders

UCL Institute of Neurology

University College London

Queen Square, London, WC1N 3BG, UK

Email: l.zrinzo@ucl.ac.uk

Fax: +44 (0) 20 3108 0142

Tel: +44 (0) 20 3108 0026

This large observational study presents long term clinical results after stereotactic radiofrequency ablation of the anterior limb of the internal capsule in 76 adults with severe life threatening anorexia nervosa (AN) refractory to other locally available treatments. The rationale for this approach was the observation that BMI had increased following anterior capsulotomy in patients with obsessive compulsive disorder (OCD) and comorbid AN.(1)

Three year follow up data was available in 74 of 76 patients: body mass index (BMI) had increased from 13.6 ± 1.6 to 19.3 ± 3.6 kg/m² ($P < 0.001$), with 46 patients reaching a “healthy” BMI of ≥ 18.5 kg/m²; the Yale-Brown Obsessive Compulsive Score had improved from 19.3 ± 8.9 to 10.9 ± 10.1 ($P < 0.001$); and there was a significant improvement in validated scores of anxiety, depression and social function. Long term adverse events were disinhibition (6 patients), memory loss (3 patients) and lethargy (4 patients), although the severity of these was not described.

There are several limitations of the study, including the lack of a control group and disease specific scales to analyse the important cognitive and behavioural aspects of AN. Nevertheless, concomitant improvements in anxiety, depression and social function suggest that anterior capsulotomy does not simply cause weight gain, but may also address the underlying psychopathology.

The reversibility of deep brain stimulating (DBS) makes it an appealing option when exploring novel indications and brain targets in mental health disorders and DBS in AN is also being explored.(2) Indeed, the modern era of stereotactic surgery for mental health disorders started in 1999 with the first published reports of DBS for severe refractory obsessive compulsive disorder (OCD) and Tourette syndrome (3,4) with efficacy demonstrated in small randomised controlled trials.(5,6) Nevertheless, the number of reported patients undergoing DBS for mental health disorders remains vanishingly small,

especially when compared to the healthcare burden imposed by these conditions. There are many reasons why this may be the case, including a general lack of interest in neurosurgical therapies by psychiatrists as well as the cost of DBS hardware and labour-intensive follow-up.

In this context, it is worth noting that DBS is not necessarily superior to stereotactic ablation for mental health disorders. Indeed, anterior capsulotomy may actually offer distinct advantages over “capsular region” DBS in OCD, both in terms of safety and efficacy.⁽⁷⁾ In anorexia nervosa, specific advantages of ablation include avoidance of general anaesthesia in metabolically fragile patients and the negative effect on body image associated with an implanted pulse generator.

The ethical challenges are considerable when contemplating surgical research on such vulnerable patient groups.⁽⁸⁾ These concerns should not terminate with the proposed study. Consideration should also be given to the likelihood of the surgical therapy becoming widely available to those in need, if found to be effective.

The authors are to be commended for trying to assist these severely affected individuals in difficult circumstances and for producing this timely manuscript that should encourage others to explore this line of enquiry. Ethical research into DBS and stereotactic ablation for anorexia nervosa can and should proceed in parallel.

References

1. Barbier J, Gabriëls L, Van Laere K, Nuttin B. Successful anterior capsulotomy in comorbid anorexia nervosa and obsessive-compulsive disorder: case report. *Neurosurgery*. 2011 Sep;69(3):E745–51–discussionE751.
2. Lipsman N, Lam E, Volpini M, Sutandar K, Twose R, Giacobbe P, et al. Deep brain stimulation of the subcallosal cingulate for treatment-refractory anorexia nervosa: 1 year follow-up of an open-label trial. *Lancet Psychiatry*. 2017 Apr;4(4):285–94.

3. Nuttin B, Cosyns P, Demeulemeester H, Gybels J, Meyerson B. Electrical stimulation in anterior limbs of internal capsules in patients with obsessive-compulsive disorder. *The Lancet*. 1999 Oct;354(9189):1526.
4. Vandewalle V, van der Linden C, Groenewegen HJ, Caemaert J. Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. *The Lancet*. 1999 Feb;353(9154):724.
5. Kefalopoulou Z, Zrinzo L, Jahanshahi M, Candelario J, Milabo C, Beigi M, et al. Bilateral globus pallidus stimulation for severe Tourette's syndrome: a double-blind, randomised crossover trial. *The Lancet Neurology*. 2015 Jun;14(6):595–605.
6. Mallet L, Polosan M, Jaafari N, Baup N, Welter M-L, Fontaine D, et al. Subthalamic nucleus stimulation in severe obsessive-compulsive disorder. *N Engl J Med*. 2008 Nov 13;359(20):2121–34.
7. Pepper J, Hariz M, Zrinzo L. Deep brain stimulation versus anterior capsulotomy for obsessive-compulsive disorder: a review of the literature. *Journal of Neurosurgery*. 2015 May;122(5):1028–37.
8. Park RJ, Singh I, Pike AC, Tan JOA. Deep Brain Stimulation in Anorexia Nervosa: Hope for the Hopeless or Exploitation of the Vulnerable? The Oxford Neuroethics Gold Standard Framework. *Front Psychiatry*. 2nd ed. 2017 Mar 20;8(8):135–10.