www.surgicalneurologyint.com

ScientificScholar® Knowledge is power
Publisher of Scientific Journals

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuropsychiatry

Editor
Miguel Faria MD
President, Hacienda Publishing, Inc., USA

SNI Open Access

Case Report

Refractory anorexia nervosa in adulthood and nucleus accumbens deep brain stimulation

Monica Lara-Almunia[1], Iratxe Aguirre-Orue[2], Carolina Roset-Ferrer[2], Carmen Bermudez-Andion[2], Ana Sofia Alvarez[1], Antonio Mas-Bonet[3], Jose Miguel-Pueyo[2], Javier Hernandez-Vicente[4]

[1]Department of Neurosurgery, Jimenez Diaz Foundation University Hospital, Madrid, Departments of [2]Psychiatry and Psychology and [3]Radiology, Son Espases University Hospital, Palma, [4]Department of Neurosurgery, University Hospital of Salamanca, Salamanca, Spain.

E-mail: *Monica Lara-Almunia - mnclr23@gmail.com; Iratxe Aguirre-Orue - irache.aguirre@ssib.es; Carolina Roset-Ferrer - carolina.roset@ssib.es; Carmen Bermudez-Andion - carmenm.bermudezdelapuent@ssib.es; Ana Sofia Alvarez - anasofialvarez@gmail.com; Antonio Mas-Bonet - antonio.mas@ssib.es; Jose Miguel-Pueyo - josem.demiguel@ssib.es; Javier Hernandez-Vicente - hodghkin@hotmail.com

***Corresponding author:**
Monica Lara-Almunia,
Department of Neurosurgery,
Jimenez Diaz Foundation
University Hospital, Madrid,
Spain.
mnclr23@gmail.com

Received : 10 December 2022
Accepted : 01 January 2023
Published : 20 January 2023

DOI
10.25259/SNI_1112_2022

Quick Response Code:

ABSTRACT

Background: Anorexia Nervosa is a life-threatening mental illness with numerous consequences. Some cases are chronic and refractory to multiple treatments. Consequently, there is great interest in therapeutic alternatives that may improve severe patients. We present an adult patient with anorexia nervosa that underwent to bilateral nucleus accumbens deep brain stimulation (NAc-DBS).

Case description: The patient was a healthy 46-year-old woman with higher education and an adequate premorbid socio-labour situation. Her disease had a late onset (25 years). The patient never presented clinical remission or weight stability. In recent years, the patient's body mass index (BMI) was 13.16 (32kg). The case was evaluated with multiple neuropsychological tests as well as the BMI before and after surgery. The clinical follow-up was 50 months. After bilateral NAc-DBS the patient experienced an important clinical benefit and significant improvement in neuropsychological tests and weight (BMI 17.28, 42 kg; 50th month) Programming: 4,5V, 130Hz, 210 μs.

Conclusion: Despite the patient´s age and the long duration of the disease, our results suggest that bilateral nucleus accumbens stimulation may be a useful and effective therapeutic strategy for cases such as the one presented. Additionally, this case presents a surgical midlife patient with both the latest disease onset and the longest follow-up after treatment in the literature.

Keywords: Anorexia nervosa, Deep brain stimulation, Nucleus accumbens, Stereotactic surgery

INTRODUCTION

Anorexia nervosa (AN) is a serious psychiatric disorder characterized by a restriction of food intake and other characteristic symptoms. It leads to significant weight loss and consequently, to physical and psychosocial deterioration. AN has a prevalence of 0.3–2.2% among the population. This disease usually begins in adolescence (15–19 years) with a higher incidence in females (10:1).[8] The long-term mortality rate of AN is nearly 20%, which represents the highest mortality rate of all psychiatric disorders. This mortality is usually caused by heart failure or suicide.[1,18] For this reason, and due to the risk of evolution toward chronicity, both an early diagnosis and the optimization of the treatment for each case are crucial.

The first line of treatment is nutrition to restore a healthy weight and psychotherapy to modify cognitive and behavioral patterns. However, nearly 50% of cases develop a refractoriness to conventional treatments, producing relapse episodes with a global and progressive deterioration. Few effective and enduring treatments are available for refractory AN.[7] Surgical treatment, including ablative procedures and deep brain stimulation (DBS), has induced mixed results and is rarely considered for these drug-resistant patients.[10]

We present a case of an adult patient with refractory, chronic, and severe restrictive AN, who was submitted to bilateral nucleus accumbens DBS (NAc-DBS). The primary goal was to assess the safety and acceptability of the procedure. The secondary goals were to analyze changes in body-mass index (BMI), anxiety, mood, obsessive symptoms, quality of life affective regulation, and AN-specific behaviors. According to the literature review, 41 cases[13,20] with NAc-DBS have been published worldwide. In relation to this series, our case is the surgical midlife patient with both the latest onset of the disease and the longest follow-up after NAc-DBS.

METHODS

Clinical case

The patient is a 46-year-old woman with no relevant medical history and the eldest of three siblings. She graduated from university studies and has an adequate premorbid sociolabor situation. Her illness had a late onset at the age of 25 and worsened after her mother's death, when she was 35-years-old. Since then, there have been numerous voluntary and involuntary hospital admissions, some of which required judicial authorization. Enteral feeding by nasogastric tube was necessary on several occasions due to food intake refusal.

Throughout disease evolution, the patient never presented clinical remission nor weight stability. Clinical examination before the intervention noted general deterioration, weakness, dizziness, pain, vascular fragility, bruising, cold extremities, hypothermia, leg edema, dermatological lesions, angular stomatitis, frequent falls, sudden sleepiness, intermittent abdominal pain, and amenorrhea. Moreover, further blood analysis showed signs of liver inflammation, a severe protein-calorie malnutrition, pancytopenia, anemia (Hb 10.4), hypoglycemia, and ionic deficiency. Radiologic examination described significant osteopenia. The patient's usual body mass index (BMI) was 13.16 (32 kg) and her lowest recorded weight was 29 kg (BMI 12.7) at the age of 41. The normal BMI is 18.5–24.9. Her height was 1.56 meters.

Regarding the psychopathological level, the patient mainly suffered from body image distortion, phobic fear of weight gain, partial disease awareness, cleaning rituals, and ritualized obsessive behaviors related to her diet. Her usual medical treatment included selective serotonin reuptake inhibitors, benzodiazepines, and antipsychotics.

The case was studied by a multidisciplinary committee and the neurosurgical intervention was authorized by the Ethics Committee and the Hospital Center's Management (compassionate use). The DBS implantation took place in September 2018.

Surgical technique

Initially, the patient underwent a period of general condition stabilization. Later, bilateral NAc-DBS was performed. A 3T- MRI scan (General Electrics®, USA) was done two weeks before the surgery, with FLAIR and contrast enhanced T1-weighted images. Axial cuts were made of 1 mm in thickness consecutively through the entire head. This neuroimaging test showed normal brain structures. The surgical procedure involved the implantation of the Leksell G stereotactic head frame under local anesthesia. This was followed by a stereotactic 64-slice CT scan (General Electrics®, USA). MRI and CT images were downloaded and fused into the Stealth Station S7 surgiplan system (Medtronic®). The anterior and posterior commissures were marked, and calculations (anatomical planning and direct visualization) were made for NAc on both sides. The final coordinates, from the midcommissural point, were ($x = 7.63$; $y = 18.03$; $z = -4.15$) on the right side and ($x = -7.61$; $y = 18.01$; %) on the left side. In the operating room, bilateral NAc-DBS electrodes (Model 3389, Medtronic®, USA) were inserted into the brain under local anesthesia and sedation. Macrostimulation was used to evaluate potential side effects. The frame was then removed, and the electrodes were connected to a subclavicular battery (Model Activa RC, Medtronic®, USA), under general anesthesia. Finally, bandages were applied and the patient was moved to the recovery room in a stable condition. There were no complications during the procedure. A brain 3D CT scan 24 h after the intervention showed normal postsurgical changes and confirmed correct electrode positioning according to preoperatory planning.

Clinical and neuropsychological evaluation

The patient was monitored in the neurosurgery department and discharged 1 week later. Clinical assessments were performed before and after surgery monthly. Members of the psychiatry and neurosurgery team evaluated the patient. Repeated blood tests and BMI measurements were performed.

The neuropsychological evaluation was completed before and after DBS device activation at the 6-month and 50-month follow-ups. The patient underwent psychometric assessments including State Trait Anxiety Inventory for anxiety, Beck Depression Inventory for depression, Yale-Brown obsessive compulsive scale for obsessive compulsive disorder (OCD), health-related quality of life (SF-36), Derogatis' Symptom Checklist Revised (SCL-90-R) for psychological symptoms and distress, and Eating Disorder Inventory-3 (specific scales).

Statistical analysis was carried with SPSS 25.0 for Windows (SPSS Inc, Chicago, Illinois, USA).

RESULTS

The stimulation was switched on 14 days after surgery. Both lowest contacts, contacts 0 and 8 (Model 3389, Medtronic®, USA), were activated at 2.5V, 130Hz, 210 µs and voltage was progressively increased to 4.5 V during the 1st month.

After 6 months, the patient's BMI experienced a relevant increase from the presurgery baseline BMI of 13.16 (32kg) to a BMI of 17.55 (43 kg); this improvement was maintained at the 50-month postsurgical follow-up, when the BMI was 17.28 (42 kg).

After intervention, the scores for anxiety, depression, OCD, quality of life, social functioning, and eating disorder specific scales were shown to have improved significantly at both the 6-month and 50-month follow-ups.

No transitional or permanent neurosurgical complications were noted after the treatment.

The results are shown in Figure 1 and Table 1.

DISCUSSION

AN was first described in the 17th century and later established in the 19th century. Although the disorder has been recognized for centuries, AN remains among the most challenging psychiatric conditions to treat.[15]

The etiopathogenesis of AN is complex and not fully understood. At present, the most accepted theory describes a multifactorial origin, attributing the development and maintenance of the disorder to a combination of environmental, genetic, and personality-based factors.[22]

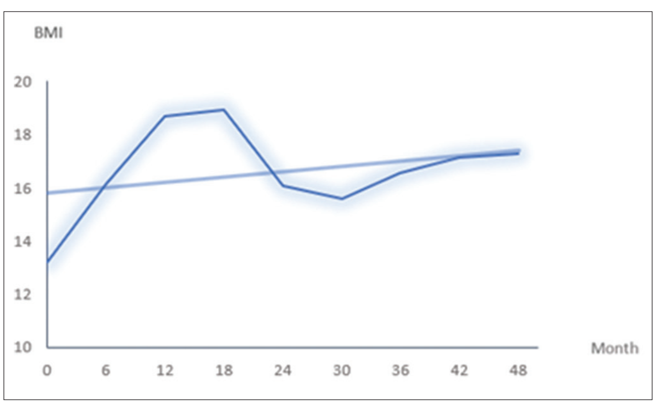

Figure 1: Body mass index.

Patients with severe AN require admission to specialized units which results in a high health-care-associated cost burden. To date, clinical interventions only have marginal success in altering the natural history for most cases. Consequently, there is an urgent need for novel therapeutic strategies.

The use of neurosurgical techniques as a treatment for mental pathologies in psychiatry began in the first half of the 20th century. Initially, surgical options in patients with AN involved ablative procedures by means of prefrontal leucotomy[6,17] or stereotactic ablation of different brain structures.[3,24] Later, technological advances contributed to safer and more effective neurosurgical approaches such as DBS. In contrast to ablative procedures, DBS is a reversible and nonlesional technique, which allows stimulation parameters to be individually adjusted. The first published case of DBS in AN appeared in 2011, for a patient with comorbid major depression.[9] Since then, only 69 patients have undergone DBS for AN using different targets.[2,9,13,19,25]

Recent advances in genetics, neuroimaging, and preclinical models have shed light on the mechanisms and circuits that drive the condition.[22] These results help to explain the heterogeneous nature of the disease and its high rate of comorbidity with other axis I disorders. Therefore, areas such as the bed nucleus of the stria terminalis involved in generalized anxiety disorder,[12] the subcallosal cingulate cortex (SCC) related to major depressive disorder,[5] and nucleus accumbens (NAc) involved in OCD, have been shown to be affected in patients who had anorexia coupled with these conditions.[12] Consequently, the modulation of nuclei involved in reward circuits with DBS techniques constitutes a rational treatment strategy. In this context, regarding the treatment for refractory AN, authors such as Israel *et al.*[9] and Lipsman *et al.*[10] stimulated the SCC, while colleagues like Barbier *et al.*,[3] McLaughlin *et al.*[14] and Blomsted *et al.*[4] stimulated areas of the striatum. All of them showed promising improvements in AN symptomatology.

The target used in this procedure is the NAc. The nucleus accumbens is part of the basal ganglia. It lies in the rostral cerebral hemisphere, in the ventral forebrain. This nucleus is a major component of the ventral striatum, is situated between the putamen and the caudate nucleus, and has a close relation to the base of septum pellucidum. Morphologically, the nucleus accumbens has been shown to be longest along its anterior-posterior axis and shortest on the dorsal-ventral axis. It is divided into two functionally distinct subregions: a shell region which is related to the limbic system, and a central core region which is related to the extrapyramidal motor system. Regarding neurophysiology, the nucleus accumbens receives, between others afferent projections, dopaminergic projections from the ventral tegmental area and substantia nigra of the midbrain. This connection forms part of a major dopaminergic pathway called the mesolimbic

Table 1: Data for psychometric assessments.

	Preoperatory (♀ 46 y)	Postoperatory (6 months)	Postoperatory (50 months)	Improvement (% pre-post)
Anxiety (STAI)				
State anxiety	75	50	48	36%
Trait anxiety	45	30	9	80%
Depression (BDI)	35	25	15	57.1%
Obsessive compulsive disorder (YBOCS)				
Obsessive symptoms	18	3	4	77.7%
Compulsive symptoms	19	7	9	52.6%
Quality of life (SF-36)				
Physical functioning	55	100	98	78.1%
Role limitations: physical health	0	100	100	100%
Pain	63	70	100	58.7%
Social functioning	50	75	100	50%
Emotional well-being	40	52	79	97.5%
Role limitations: emotional problems	0	100	100	100%
Energy/fatigue	55	70	93	69.9%
General health	75	80	87	16%
Health change	100	100	100	0%
Psychological symptoms and distress (SCL-90-R)				
Somatizations	2.25	2.05	1.35	40%
Obsessions and compulsions	2.8	2.3	1.9	32.1%
Interpersonal sensitivity	3.1	3.1	2.5	19.3%
Depression	3.62	3.5	2.11	41.7%
Anxiety	2.6	1.9	1.2	53.8%
Hostility	1.67	1.33	1.1	34.1%
Phobic anxiety	2.14	3	1.1	48.5%
Paranoid ideation	1.17	2.67	1.2	0%
Psychoticism	2	2.1	1.62	19%
Global severity index	2.52	2.74	1.51	40%
Eating disorders (EDI-3; specific scales)				
Drive for thinness	63	63	53	15.8%
Bulimia	76	91	65	14.4%
Body dissatisfaction	43	59	51	0%
Risk index	64	77	59	7.8%

*STAI: State trait anxiety inventory; BDI: Beck depression inventory; YBOCS: Yale-Brown obsessive compulsive scale; SF-36: Health-related quality of life; SCL-90-R: Derogatis' symptom checklist revised; EDI-3: Eating disorder inventory-3; ♀ Woman

pathway. As a consequence, it is a key part of the reward system and this nucleus has also been recognized as an important part of the systems that modulate motivationally-facilitated behavior, addiction, feelings, and processing of aversive events. In this way, the available experience suggests that the NAc is a relevant target for the surgical treatment of different mental disorders such as OCD or anorexia.[16] In fact, the dysfunction of this nucleus is associated with altered circuits of OCD. The bilateral NAc-DBS for OCD is already approved in Europe as treatment for drug-resistant cases. In relation to eating disorders, Wang *et al.*[21] analyzed glucose metabolism in AN, finding significant metabolic changes mainly in the frontal lobe, lentiform nucleus, limbic cortex, pons, and parietal lobe. They hypothesized that these regions could be keystones in neurocircuits related to appetite and observed that NAc-DBS modulated some of the abnormal metabolic brain regions. At present, 41 cases with refractory AN and NAc-DBS have been published worldwide.[13,20]

Wang *et al.*,[21] Wu *et al.*,[23] and Zhang *et al.*[24] noticed that the cases of adolescent patients with short-term AN refractory to medical treatment (<4 years) improved their BMI after NAc-DBS. The most extensive series in the literature, with a total of 28 women with refractory AN who underwent NAc-DBS, showed significant increase in BMI and improvement in psychiatric scales scores at their 6-month follow-up. These scores were maintained at the 2-year follow-up. In addition, they observed that the NAc-DBS stimulation was more effective for weight restoration in patients with the restrictive subtype of AN than in those with the binge-eating/purge subtype.[11] However, adult patients with refractory anorexia presented mixed responses. Consequently, while Wang *et al.*[21] describe weight gain after

DBS in a 26-year-old adult patient with refractory anorexia with 2 years of evolution, Martínez *et al*.[20] found no statistically significant difference between preoperative BMI and BMI 6 months postsurgery for four adult patients with refractory anorexia with over 10 years of evolution, treated with bilateral stimulation of the nucleus accumbens ($P = 0.84$).

In our case, the patient was an adult with a very late disease onset (25 years old) and over 20 years of evolution. On the presurgical neuropsychological scales, she presented scores consistent with generalized anxiety disorder, severe depression, and particularly severe OCD regarding cleaning habits and ritualized obsessive behaviors related to her diet. Both the presurgical neuropsychological status of the patient and the known functions of the nucleus accumbens, determined the multidisciplinary committee's decision regarding the final choice of the target. After 50 months from the NAc-DBS, all neuropsychological scales improved significantly, and among other findings, the patient's scores were comparable with mild depression and mild OCD. The patient presented a significant decrease in her obsession levels, which improved her ritualized dietary behaviors. Consequently, she experienced a progressive BMI recovery and a better nutritional status.

However, as with most studies on DBS for AN,[10,14,21] our patient did not improve her distorted body image perception (body dissatisfaction). Furthermore, during the home confinement of the COVID-19 pandemic, the patient showed a decline in her BMI, from which she recovered progressively [Figure 1].

Concerning possible complications associated with this type of surgical intervention, no neurological adverse effects, bleeding, or death have been described in any published Anorexia case treated with DBS to date.[11,19,20] These procedures are performed by neurosurgeons experienced in DBS techniques that present low rates of DBS-related complications. In our case, there were no immediate complications associated with the surgical intervention (e.g., neurological deficit and hemorrhage), the incision (e.g., infection and dehiscence), or in the stimulation system after 12 months of follow-up.

A review of the literature (NAc-DBS for intractable anorexia) is showed in Table 2.

Table 2: Review, anorexia, case reports, and series with bilateral stimulation of nucleus accumbens.

Author	No. Patients	Age (years)/ Gender	Duration of disease (years)	Comorbid neuropsychiatric disorders	Treatment	BMI (pre-surgery)	Follow-up (months)	BMI (post -surgery)
Wu *et al*.[23]	Case 1	14/Female	2.3	OCD	SSRIs, Olanzapine	12.2	48	22.1
	Case 2	15/Female	1.5	OCD	SSRIs, Olanzapine	13.3	48	18.4
	Case 3	16/Female	1.25	Generalized anxiety disorder	SSRIs, Olanzapine	12	48	18.5
	Case 4	15/Female	1.08	OCD	SSRIs, Olanzapine	10	9	19.4
Zhang *et al*.[25]	Case 1	17/Female	1.08	---	SSRIs	11.8	1	17.9
	Case 2	13/Female	3.5	---	SSRIs	12.2	1	17.1
Wang *et al*.[21]	Case 1	26/Female	2	OCD, Depression, Anxiety	---	13.3	12	18
	Case 2	15/Female	3	OCD, Depression, Anxiety	---	12.9	12	20.8
Martínez *et al*.[20]	Case 1	45/Male	31.8	Anxiety	None	13.44	6	17.51
	Case 2	39/Female	25	Anxiety	Benzodiazepines	11.47	6	12.55
	Case 3	57/Female	41	Anxiety	SSRI Benzodiazepines	11.92	6	12.74
	Case 4	34/Female	19	Anxiety	Benzodiazepines	11.61	6	12.34
Liu *et al*.[11]	28 Cases	22.8 ± 4.1/ Female	5.1 (3–10)	----	SSRI Phychotherapy	13.01 ± 1.86	24	15.29 ± 2.28
Arroteia *et al*.[2]	Case 1	42/Female	26	Depression	Phychotherapy	12.8	24	18.82
Present Study (2022)	Case 1	46/Female	21	OCD, Depression, Anxiety	SSRIs, Benzodiazepines Olanzapine	13.16	50	17.28

BMI: Body mass index, OCD: Obsessive compulsive disorder, SSRI: Selective serotonin reuptake inhibitors

CONCLUSION

AN is an important health problem in industrialized countries, associated with high morbidity and mortality, as well as high health-care costs.

In our case, the surgical intervention achieved a significant decrease in preoperative obsessiveness levels and positive changes in habitual nutritional behaviors. Consequently, there was a progressive improvement in the patient's BMI and nutritional status, a decrease in her anxiety-depressive symptoms, and ultimately, an improvement in her overall quality of life. Therefore, both our results and those from most published articles suggest that bilateral stimulation of the nucleus accumbens may constitute a safe, useful, and effective therapeutic strategy for cases such as the one presented. These results remain consistent in our patient despite the late age at which the disease began and the long period of evolution before the procedure.

Recent technological advances and their adaptation to the neurosurgical field facilitate this type of intervention. Nevertheless, to optimize results and minimize risks, a multidisciplinary team must work in conjunction with neurosurgeons experienced in this type of surgical intervention to conduct a detailed study and make an appropriate determination of the patient's target.

Acknowledgments

I thank senior author (JHV M.D., Ph.D), for his dedication, ideas, and excellent labor as a neurosurgeon. My career trajectory would not have been possible without him.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders. Arch Gen Psychiatry 2011;68:724-31.
2. Arroteia IF, Husch A, Baniasadi M, Hertel F. Impressive weight gain after deep brain stimulation of nucleus accumbens in treatment-resistant bulimic anorexia nervosa. BMJ Case Rep 2020;13:e239316.
3. Barbier J, Gabriels L, van Laere K, Nuttin B. Successful anterior capsulotomy in comorbid anorexia nervosa and obsessive-compulsive disorder: Case report. Neurosurgery 2011;69:745-51.
4. Blomstedt P, Naesström M, Bodlund O. Deep brain stimulation in the bed nucleus of the stria terminalis and medial forebrain bundle in a patient with major depressive and anorexia nervosa. Clin Case Rep 2017;5:679-84.
5. Broadway JM, Holtzheimer PE, Hilimire MR, Parks NA, Devylder JE, Mayberg HS, *et al*. Frontal theta cordance predicts 6-month antidepressant response to subcallosal cingulate deep brain stimulation for treatment-resistant depression: A pilot study. Neuropsychopharmacology 2012;37:1764-72.
6. Drury MO. An emergency leucotomy. Br Med J 1950;2:609.
7. Fichter MM, Quadflieg N, Hedlund S. Twelve-year course and outcome predictors of anorexia nervosa. Int J Eat Disord 2006;39:87-100.
8. Hoek HW. Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. Curr Opin Psychiatry 2006;19:389-94.
9. Israel M, Steiger H, Kolivakis T, McGregor L, Sadikot AF. Deep brain stimulation in the subgenual cingulate cortex for an intractable eating disorder. Biol Psychiatry 2010;67:53-4.
10. Lipsman N, Lam E, Volpini M, Sutandar K, Twose T, 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;4:285-94.
11. Liu W, Zhan S, Li D, Lin Z, Zhang C, Wang T, *et al*. Deep brain stimulation of the nucleus accumbens for treatment-refractory anorexia nervosa: A long-term follow-up study. Brain Stimul 2020;13:643-9.
12. Luyten L, Casteels C, Vansteenwegen D, van Kuyck K, Koole M, van Laere K, *et al*. Micro-positron emission tomography imaging of rat brain metabolism during expression of contextual conditioning. J Neurosci 2012;32:254-63.
13. Mahoney JJ, Koch-Gallup N, Scarisbrick DM, Berry JH, Rezai AR. Deep brain stimulation for psychiatric disorders and behavioral/cognitive-related indications: Review of the literature and implications for treatment. J Neurol Sci 2022;15:120253.
14. McLaughlin NC, Didie ER, Machado AG, Haber SN, Eskandar EN, Greenberg BD. Improvements in anorexia symptoms after deep brain stimulation for intractable obsessive-compulsive disorder. Biol Psychiatry 2022;73:29-31.
15. Pearce JM. Richard Morton: Origins of anorexia nervosa. Eur Neurol 2004;52:191-2.
16. Salgado S, Kaplitt MG. The nucleus accumbens: A comprehensive review. Stereotact Funct Neurosurg 2015;93:75-93.
17. Sargant W. Leucotomy in psychosomatic disorders. Lancet 1951;2:87-91.
18. Smink FR, van Hoeken D, Hoek HW. Epidemiology of eating disorders: Incidence, prevalence and mortality rates. Curr Psychiatry Rep 2012;14:406-14.
19. Sobstyl M, Stapińska-Syniec A, Sokół-Szawłowska M, Kupryjaniuk A. Deep brain stimulation for the treatment of severe intractable anorexia nervosa. Br J Neurosurg 2019;33:601-7.

20. Villalba Martínez G, Justicia A, Salgado P, Ginés JM, Guardiola R, Cedrón C, *et al*. A randomized trial of deep brain stimulation to the subcallosal cingulate and nucleus accumbens in patients with treatment-refractory, chronic, and severe anorexia nervosa: Initial results at 6 months of follow up. J Clin Med 2020;9:1946.
21. Wang J, Chang C, Geng N, Wang X, Gao G. Treatment of intractable anorexia nervosa with inactivation of the nucleus accumbens using stereotactic surgery. Stereotact Funct Neurosurg 2013;91:364-72.
22. Wood L, Al-Khairulla H, Lask B. Group cognitive remediation therapy for adolescents with anorexia nervosa. Clin Child Psychol Psychiatry 2013;16:225-31.
23. Wu H, Van Dyck-Lippens PJ, Santegoeds R, van Kuyck K, Gabriëls L, Lin G, *et al*. Deep-brain stimulation for anorexia nervosa. World Neurosurg 2013;80:S29.e1-10.
24. Zamboni R, Larach V, Poblete M, Mancini R, Mancini H, Charlin V, *et al*. Dorsomedial thalamotomy as a treatment for terminal anorexia: A report of two cases. Acta Neurochir Suppl (Wien) 1993;58:34-5.
25. Zhang HW, Dian-You L, Zhao J, Guan YH, Sun BM, Zuo CT. Metabolic imaging of deep brain stimulation in anorexia nervosa A 18F-FDG PET/CT study. Clin Nucl Med 2013;38:943-8.

How to cite this article: Lara-Almunia M, Aguirre-Orue I, Roset-Ferrer C, Bermudez-Andion C, Alvarez AS, Mas-Bonet A, *et al*. Refractory anorexia nervosa in adulthood and nucleus accumbens deep brain stimulation. Surg Neurol Int 2023;14:14.