

Deep brain stimulation in obsessive-compulsive disorder – case report of two patients

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Summary

Obsessive-compulsive disorder (OCD) occurs in 2–3% of the general population. Due to its chronicity and high resistance to standard treatment, alternative clinical management based on neuroscientific findings has been sought. Deep brain stimulation (DBS) is a modern and dynamic approach in the treatment of OCD giving hope to patients who are resistant to current pharmacotherapy and psychotherapy based treatments. This paper presents two cases of patients diagnosed with refractory OCD who received DBS therapy with concurrent pharmacotherapy and cognitive behavioral psychotherapy (CBT). Both patients underwent a neurosurgical procedure to implant electrodes into the anterior limb of the internal capsule (ALIC) and nucleus accumbens (NAc). Before and after the start of the neurostimulation, patients underwent a clinical evaluation which consisted of a psychiatric examination and psychometric measurements (Y-BOCS, HAMA, HDRS, GAF, SOFAS). During the follow-up period, a blind attempt to switch off the neurostimulation was made. During the 6-month follow-up period, a significant reduction in the obsessive-compulsive, depressive and anxiety symptoms was achieved as well as an improvement in global patient functioning. The tolerance of DBS was found to be very good and no significant side effects were observed. The obtained results provide the basis for the implementation of this method in patients with OCD who are resistant to current treatment.

Key words: treatment-resistant obsessive-compulsive disorder, deep brain stimulation

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder with a high resistance to standard treatment (up to 30%). It is in fourth place in terms of prevalence of mental disorders in the general population. OCD affects roughly 2.3%

of the population, while between 6 and 8% of the population demonstrate subclinical symptoms [1]. The chronicity of the illness process, severity and resistance to standard treatment places a large burden on the patients and their families resulting in a state of disability and social exclusion in about 10% of patients [2]. Deep brain stimulation (DBS) or neurosurgical ablation could potentially help alleviate symptoms associated with OCD. In this paper we present an analysis of the course of therapy of two patients who underwent DBS for the treatment of OCD.

Standard treatment of OCD includes pharmacotherapy with antidepressants as well as cognitive behavioral therapy (CBT). The first-line drugs for the treatment of OCD are antidepressants from the group known as selective serotonin reuptake inhibitors (SSRIs), given at maximum doses for at least 12 weeks. If the treatment is found to be ineffective, clomipramine is then used. Hirschtritt et al. [3] conducted a large-scale meta-analysis of controlled randomized OCD pharmacotherapy trials and found that the effectiveness of SSRIs in reducing the severity of symptoms was confirmed in between 40 and 60% of patients. This group includes patients (so-called responders) whose clinical improvement was determined on the basis of a 25% reduction in the number of points in the *Yale-Brown Obsession and Compulsion Scale* (Y-BOCS). Attention was also drawn to the positive effect of SSRI augmentation with antipsychotic drugs (most commonly risperidone) and the importance of CBT [3].

2. Cognitive behavioral therapy in OCD

The effectiveness of cognitive and behavioral techniques in reducing the symptoms of OCD has been the subject of research for several decades [4]. Cognitive behavioral therapies usually combine cognitive techniques with exposure and ritual prevention techniques (EX/RP) and are currently considered to be the most effective in the treatment of OCD [5, 6], recommended by both the National Institute for Health and Care Excellence (NICE) [7] and the American Psychiatric Association (APA) [8]. In the context of the research into the effectiveness of DBS in the treatment of OCD, more and more authors have begun to emphasize CBT therapy as a complementary method to neurosurgical intervention. In a study by Mantione et al. [9] (2014), the authors postulated and confirmed the hypothesis that the addition of CBT interventions increases the effectiveness of DBS in the reduction of compulsive symptoms.

3. DBS therapy

In Poland (including the Department of Neurosurgery, University Clinical Hospital in Wrocław) and overseas, DBS is used in the treatment of neurological disorders such as Parkinson's disease as well as a number of motor dysfunctions (such as essential tremor or dystonias). However, more and more centers in the world, especially in the USA and Europe, use this method to treat mental disorders. In the US, DBS has been

registered in the treatment of OCD by the FDA since 2008. In Poland, pioneering DBS treatments in patients with OCD were performed by professor Marek Harat from the Department of Neurosurgery at the Military Clinical Hospital in Bydgoszcz.

DBS is a minimally invasive surgical procedure allowing direct modification of the activity of neuronal centers and circuits in a gradual and reversible manner. It was developed on the basis of ablative methods [10]. The first use of DBS as a therapeutic method used temporarily in humans was documented by Bekhtereva [11] in 1963, while its use as a long-term method was published by Benabid in 1987 [12].

Numerous observations have shown that by blocking the limbic system in the striatum (anterior limb of the internal capsule – ALIC, ventral capsule and ventral striatum – VC/VS, nucleus accumbens – NAc, ventral caudate nucleus – VCN, subthalamic nucleus (STN) or the inferior thalamic peduncle – ITP) may reduce the severity of symptoms in OCD, depression and Tourette syndrome [13–18].

The first DBS surgical procedures with the intention of treating refractory OCD were performed in 1999 by Nuttin [17]. The location of the electrode placement within the ALIC was identical to the location of previous capsulotomies. Subsequent studies confirmed the effectiveness of DBS compared to ablation methods, (approximately 64%), with a significantly lower risk of side effects [19, 20]. In addition, publications have reported that there were no side effects in the treatment of OCD by DBS such as chronic frontal lobe disorders, cognitive impairment or personality changes. However, mild hypomanic states were observed [19].

4. A report of two case studies outlining the use of DBS in refractory OCD

A team of researchers from the Department and Clinic of Psychiatry and the Department and Clinic of Neurosurgery, Wroclaw Medical University, underwent specialized training at a center in Amsterdam. Two psychiatrists (Prof. Joanna Rymaszevska and Dr. Jan Aleksander Beszlej), and two neurosurgeons (Dr. Paweł Tabakow and Dr. Artur Weiser), obtained Continuing Medical Training certificates in the use of DBS in obsessive-compulsive disorder. The project was registered in the Centre for the Promotion of Research, Wroclaw Medical University, and was then approved by the Bioethical Commission for its implementation. The project is a pilot study in preparation for a larger study to assess the effectiveness and safety of DBS in patients with psychiatric disorders whose pathophysiology is associated with a disturbance of functional circuits in the brain.

OCD is often referred to as a neuropsychiatric disorder as the pathology of the cortico-striato-thalamo-cortical circuits (CSTC) was discovered on the basis of neuroscientific research. Similar reports concern other disorders including major depressive disorder (MDD, according to DSM-5 criteria).

4.1. Research methodology

Three patients with refractory OCD were recruited for the pilot study. In this paper, we present the first two patients with a diagnosis of refractory OCD, who were treated with DBS, pharmacotherapy and CBT with a six-month follow-up period after treatment.

Based on the analysis of articles published in PubMed, EMBASE, PsycINFO and training materials from the European Continuing Medical Training ('DBS & OCD', Amsterdam, Netherlands, April 2016, Course Directors – Prof. Damiaan Denys, Prof. Rick Schuurman, Chairman ECMT – Dr. Jean-Pierre Van Buyten) the following inclusion and exclusion criteria were adopted.

Table1. **Criteria for inclusion and exclusion for the use of DBS in the treatment of OCD**

Inclusion criteria:
1. Written informed consent to undergo DBS treatment.
2. Resistance (no or insufficient effect) to previous treatments, including:
– 2 treatments with selective serotonin reuptake inhibitors (SSRIs) at maximum doses for at least 12 weeks;
– one clomipramine treatment at maximum doses for at least 12 weeks;
– 1 augmentation of treatment with an atypical antipsychotic drug for at least 8 weeks;
– 1 treatment with cognitive behavioral therapy (CBT) – at least 16 therapeutic sessions.
3. Confirmation of the diagnosis and severity of the illness:
– OCD diagnosis according to DSM-5criteria;
– a score of at least 28 points in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS);
– at least five years of documented OCD treatment;
– a maximum of 45 points on the Global Assessment of Functioning Scale (GAF);
4. Other criteria:
– 18 to 65 years of age;
– IQ over 80 points.
Exclusion criteria
1. Co-morbidity of the following mental disorders:
– psychotic disorders, bipolar disorder, autism, severe personality disorders, addiction to a psychoactive substance, dementia.
2. Unstable general physical condition, including diseases of the central nervous system, such as:
– epilepsy, Parkinson's disease, multiple sclerosis.
3. Pregnancy.

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In the second stage, patients were qualified for surgery by the neurosurgical team, taking into account the contraindications listed in Table 2.

Table 2. Neurosurgical contraindications for DBS implantation

Contraindications for neurosurgical procedure:
– organic brain diseases: high degree of cortical and subcortical atrophy of the brain, hydrocephalus, a history of skull or brain surgery or brain injuries with intracranial hematomas;
– neoplasms of the body and central nervous system;
– presence of active inflammatory processes or prolonged antibiotic therapy;
– active anticoagulant therapy;
– congenital or acquired hemorrhagic diathesis (e.g., hemophilia, thrombocytopenia, vascular sclerosis);
– congenital or acquired immunodeficiency;
– unstable diseases of the cardiovascular system (ischemic heart disease, uncontrolled hypertension, atrial fibrillation);
– skin and connective tissue diseases (systemic lupus, psoriasis, atopic dermatitis, etc.);
– endocrine diseases (e.g. diabetes, unstable thyroid function, Cushing's disease and syndrome, etc.);
– asthma or COPD;
– bedsores.

4.2. Neurosurgical procedure

The neurosurgical procedure was performed to place multi-contact electrodes into the ALIC and NAc. Stimulation blocking these areas of the brain is designed to reduce pathologically hyperactive CSTC neuron circuits. Single-channel stimulators were used for the study. The electrodes were connected subcutaneously to the neurostimulators implanted in the left and right subclavian regions. Implantation of the electrodes into both hemispheres of the brain took place concurrently. The location of electrode placement was decided upon the basis of a pre-operative MR examination of the head, coordinates of the electrode placement location are available in the literature, and neurophysiological measurements (measurement of the local impedance of the brain).

Electrode implantation was performed under local anesthesia using the awake craniotomy approach (with the use of dexmedetomidine), while neurostimulator implantation was performed under full anesthesia. The position of the electrodes during the surgery was controlled intra-operatively with the help of X-ray imaging techniques. Post-operative care involved daily examination of the incision sites, up to and including suture removal.

4.3. Stimulation and evaluation of DBS effects during follow-up appointments

Stimulation was initiated up to 3 weeks after the implantation of the second stimulator. Both stimulators were activated simultaneously, initiating the stimulation in both brain hemispheres. The psychological and physical condition of the patients was regularly assessed during follow-up appointments: before the DBS procedure and every 2 weeks for the first four months, and then once a month after that. The appointments included a mental state assessment, assessment of brain stimulation parameters with possible adjustment of the stimulation parameters with the use of a dedicated programmer. The eventual correction of the stimulation parameters took place after assessment by the psychiatric team. During each appointment, an assessment of any side effects was also made. During the course of DBS, pharmacotherapy was maintained (Patient 1: sodium valproate with valproic acid – 300 mg, fluvoxamine – 300 mg, perazine – 100 mg, quetiapine – 100 mg, mirtazapine – 30 mg; Patient 2: sodium valproate with valproic acid – 900 mg, fluoxetine – 60 mg) and patients had access to CBT.

Specific scales were used to assess the following parameters:

- severity of obsessive and compulsive symptoms – *the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)* – criteria for response to treatment: a reduction of 35% of points on a scale represented a significant improvement;
- severity of depressive symptoms – *the Hamilton Depression Rating Scale (HDRS)* – Improvement criteria: a 35% reduction in points on the scale would represent a significant improvement in symptoms;
- severity of anxiety symptoms – *the Hamilton Anxiety Rating Scale (HAMA)*;
- level of social and occupational functioning – *the Global Assessment of Functioning (GAF)* or *the Social and Occupational Functioning Assessment Scale (SOFAS)*;
- personality assessment – *the Structured Clinical Interview for DSM IV – SCID-II* and the *NEO-PI-R Personality Inventory*.

5. Case 1

5.1. The pre-DBS implantation phase

Our first case is that of an unmarried, childless, 38-year-old woman, with concomitant diagnoses of Graves' disease, allergic rhinitis and luteal insufficiency. She attained a degree in pedagogic studies at university, however, she was never employed as a teacher. Her father was diagnosed with a depressive disorder and alcohol dependency, her paternal grandmother suffered from recurrent depression.

Her first symptoms of OCD appeared at the age of 16. At that time she would suffer from obsessions of an erotic nature and difficulties in decision making. Her compulsions took the form of intrusive contact and harassment of the people with whom she

had an erotic fascination (in person or by telephone) after which she would feel guilty. She also reported obsessive fears of a religious nature relating to committing sinful acts – she would then pray compulsively and attend confession several times a day. She first visited a psychiatrist aged 21, which led to a diagnosis of OCD and treatment. At this time, the patient also started the first psychotherapy. During treatment, the compulsions changed their form – the patient developed a compulsion related to frequent restroom visits to urinate, this was accompanied by repeated wiping, which would lead to bleeding. She would also repeatedly check whether the gas installation in her home was switched off or if her taps were leaking. Significant difficulties in making even trivial decisions persisted. She never undertook any form of employment after graduation, in the following years her general ability to function deteriorated. Throughout the course of the disorder, she often suffered from depressed mood and increased anxiety secondary to her OCD symptoms.

During the 17-year treatment period from her diagnosis, she was treated with fluoxetine, sertraline, citalopram, fluvoxamine, and clomipramine. Several antipsychotic drugs of both generations as well as mood stabilizers. However, pharmacotherapy and CBT only brought about a partial improvement in her symptoms.

The patient met all the criteria for the initiation of DBS therapy, including severity of symptoms (35 points on the Y-BOCS scale), severely impaired functioning (35 points on the GAF scale) and resistance to pharmacotherapy and CBT. No contraindications for the procedure were noted. After obtaining comprehensive information regarding treatment, she gave written consent for the procedure to take place.

Bilateral implantation of the electrodes into the ALIC and NAc was performed. The lowest electrode contact was placed in NAc, the other three in the ALIC. Two non-rechargeable, single channel MedtronicActiva SC neurostimulators were connected. Bilateral stimulation was initiated 3 weeks after the neurosurgical procedure. The initial parameters were: voltage 3.5 V, pulse bandwidth 90 μ s, frequency 130 Hz.

5.2. Results of the control tests

In the initial weeks of neurostimulation after surgery, there was a marked improvement in mood (HDRS), anxiety levels (HAMA) and the patient's activity scores (GAF). The severity of OCD symptoms gradually decreased, reaching their lowest level 2.5 months after the start of the neurostimulation (16 points in the Y-BOCS, a 54% improvement from baseline, which meets the criteria for treatment effectiveness), using the following parameters: voltage 4.5 V, bandwidth 150 μ s, and frequency 130 Hz. Her obsessions of an erotic and religious nature showed a reduction in intensity, however, some of the previously described compulsions remained, but with a marked reduction in intensity. The patient took up employment as a cleaner, unfortunately the employment period lasted only a few weeks. During subsequent follow-up appointments, the Y-BOCS score again increased to 26–28 points despite a further increase in

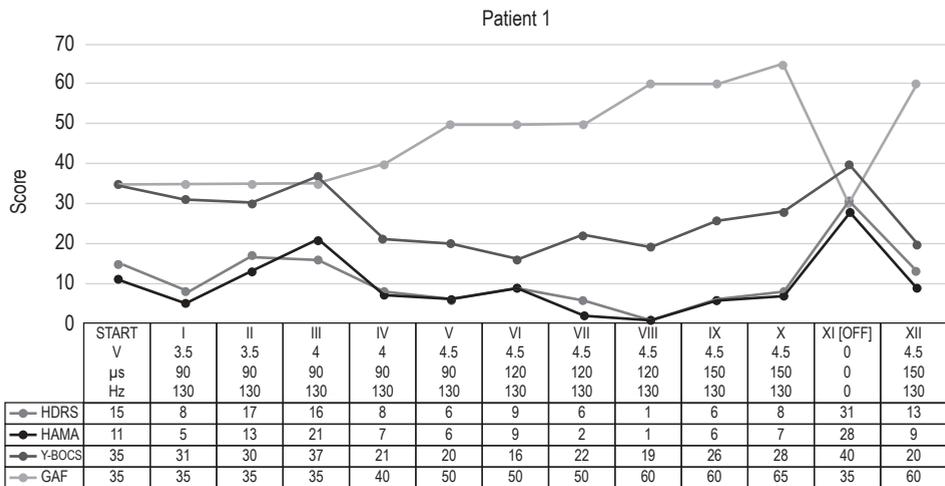


Figure 1. Results of the individual scales (HDRS, HAMA, Y-BOCS, GAF) before implantation and during the 6-month follow-up period, including stimulation parameters and values before the start of the neurostimulation (START) and after cessation of the neurostimulation – OFF

HDRS – Hamilton Depression Rating Scale; HAMA – Hamilton Anxiety Rating Scale; Y-BOCS – Yale-Brown Obsessive-Compulsive Scale; GAF – Global Assessment of Functioning

neurostimulation parameters. New obsessions occurred – related to finding a romantic partner, employment and a pet – and she would then devote several hours a day to searching the internet to fulfill these obsessions. She would also purchase dogs or adopt them from animal shelters and then return them several weeks later.

During periods of employment, the patient was assessed on the GAF scale scoring 60 points, however, the values in subsequent measurements fluctuated between 50–65 points (with a decrease to 30 points after temporary switching off the stimulation). Similar variability was observed in the HDRS and HAMA scales. On the *Hamilton Depression Rating Scale* (HDRS) used to assess depressive symptoms, the patient scored 15 points during the qualification phase of the study, this dropped to 8 points during the first evaluation conducted after the neurostimulation was initiated, and then subsequently rose to 13 points at the twelfth evaluation. The fluctuation of HDRS results during the observation period varied between 1 and 31 points, with results predominately in the range of 8–10 points. Before the start of the neurostimulation the patient scored 11 points on the HAMA scale used to assess anxiety symptoms, with a decrease of 5 points during the first evaluation after the stimulation was initiated and a further increase to 9 points at the twelfth evaluation. Fluctuation of results on the HAMA scale during the observation period fluctuated between 1 and 28 points.

5.3. Cognitive behavioral therapy

At the time of starting DBS, the patient had been undergoing therapy for several years, mainly using the integration model. She took part in the CBT program at the university center about 2 months after the start of the neurostimulation. A significant portion of the initial sessions were devoted to building the patient's motivation for therapy. The goals formulated by the patient during this period were unrealistic. There was poor cooperation during CBT sessions, the patient also reported a lack of motivation to continue treatment. She would make excuses to reschedule follow-up appointments, (e.g., a job interview on the same day) or avoid them altogether (because she 'overslept'). At home she was very inactive, spending large amounts of time in bed (up to 12 hours a day) also she was very reluctant to help her family in everyday household activities. Sleep hygiene rules were repeatedly explained to the patient, which she did not follow.

Factors hindering therapeutic work included: poor insight into the cause of her symptoms, duration of the disorder, difficulty in recalling and formulating obsessive thoughts, cognitive limitations including high attention fatigue, difficulty with focusing and maintaining attention during meetings, a tendency to passive-aggressive and avoidant behavior, such as not completing home therapy assignments. During therapeutic sessions, the patient was partially motivated to work on reducing compulsive behaviors. With the passage of time the patient became more cooperative and willingly undertook exercises involving exposure and response prevention, as well as performing independent therapy at home. Along with the increase in the number of exercises undertaken by the patient a decrease in anxiety during exposure was also observed. In the period from November to January 2018, the patient eventually participated in 10 out of 14 meetings with the CBT therapist, which gives a turnout of about 71%. Finally, after several unsuccessful attempts to make contact, the patient gave up her therapy at the end of April 2018, justifying her decision by taking another job.

5.4. Attempt to turn off the neurostimulator

At the end of the 6-month follow-up period, an attempt was made to switch off the neurostimulator. During one of the scheduled appointments, the neurosurgical team (P. Tabakow, A. Weiser) turned off the neurostimulation, without informing either the patient or the team of psychiatrists taking part in the study (J. Rymaszewska, J. Beszłej, P. Piotrowski, D. Siwicki, T. Wiczorek). The patient reported a sudden increase in anxiety and mood deterioration within a few hours of disabling the stimulator. In the following hours the frequency and severity of her obsessive-compulsive symptoms increased, and she started having suicidal thoughts. The patient was admitted to the Clinic of Psychiatry, where the stimulation was restored. On admission, the severity of OCD symptoms was estimated at 40 points on the Y-BOCS, anxiety on 28 on the

HAMA scale and depression on 31 on the HDRS (Figure 1: XI 'OFF' evaluation). After restarting stimulation, a very rapid dissipation of symptoms was observed. After hospitalization the results on the scales decreased in relation to the initial assessment: up to 20 points on the Y-BOCS (reduction of 35%), 9 points on the HAMA scale (reduction of 11 %) and 13 points on the HDRS (reduction of 13%) (Figure 1 – XII evaluation).

6. Case 2

6.1. The pre-DBS implantation phase

Patient 2 is a 28-year-old single male, childless, educated to a secondary school level, he started studying to become a paramedic but dropped out 3 times due to his OCD and issues related to social anxiety, after which he did not continue his education, nor did he pursue any form of employment. Currently he lives alone, is financially dependent on his parents, and is periodically assisted by his grandmother. He does not suffer from any physical ailments. No significant family history of mental illness was noted.

The patient reported the first onset of OCD symptoms at the age of 8, when he started experiencing obsessive thoughts of a religious and blasphemous nature. At the age of 11 years, he started experiencing symptoms of anxiety related to his obsessive thoughts, e.g., 'a fear of death', after which compulsive symptoms also appeared, including the compulsion to repeat certain activities, 'annulment rituals' (e.g., the need to raise a glass repeatedly in response to an obsessive thought related to death as not to die). The number of different types of obsessive thoughts grew with age. At around 13 he started experiencing obsessions related to a 'fear of being poisoned'. Despite attempts to hide his symptoms, over time they worsened to the point that at the age of 15 they were clearly visible to the patient's family. The aforementioned symptoms had a significant impact on his overall functioning – the amount of time spent completing day to day activities increased exponentially, e.g., coming home from school took 3 hours, preparing to leave the house or changing clothes after returning from school took about an hour. During this period, the patient was taken to see a mental health specialist, he was then diagnosed with OCD and started on pharmacological treatment.

Since the age of 15 he was treated with antidepressants (fluvoxamine, clomipramine) as well as mood stabilizers and antipsychotic medication (in order to augment the effects of SSRIs and tricyclic antidepressants). However, the treatment was found to be ineffective or only brought about short term improvement in symptom severity. The patient also undertook CBT therapy several times (2 years in total), without significant improvement.

The patient applied for the research project, mainly due to the severity of his symptoms in the form of obsessive religious thoughts and accompanying compulsive rituals, both related to the cancellation of thoughts as well as the repetition of activities

or the postponement of their performance. He also reported a significant reduction in overall functioning, inability to take up employment and social anxiety with somatic symptoms. Symptoms persisted despite the use of fluoxetine, valproate and trazodone in treatment. In psychometric tests, he scored 28 points on the Y-BOCS and 45 points on the SOFAS scale. The ineffectiveness of the previously used pharmacological and psychotherapeutic treatment was confirmed by medical documentation provided by the patient.

6.2. DBS implantation

In cooperation with a team of neurosurgeons, after excluding contraindications to perform the procedure, the patient was qualified for surgical implantation of neurostimulation electrodes for DBS. The target stimulation area was selected as in the case of the previous patient, using the same devices for neurostimulation. No complications related to the surgery were noted. Three weeks after the implantation of the second neurostimulator, neurostimulation was initiated using the following parameters: voltage 3.0V, pulse width 60 μ s, frequency 130Hz.

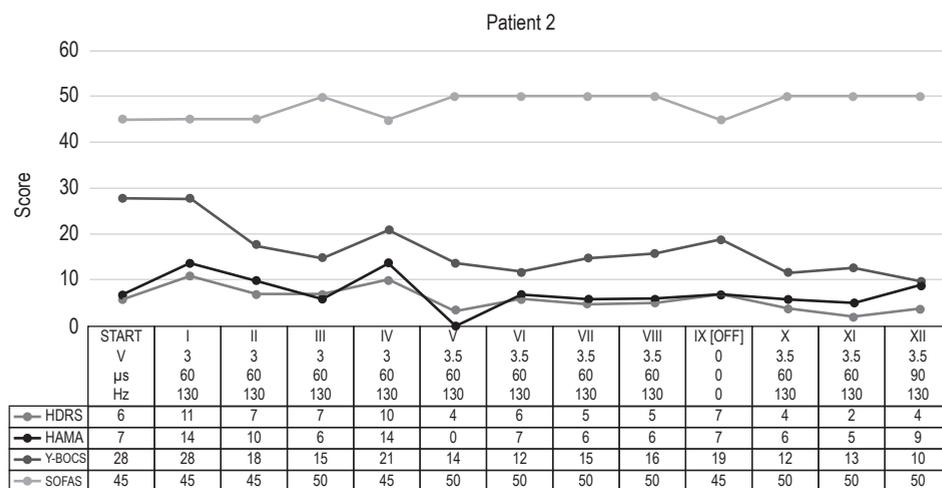


Figure 2. Results of the individual scales (HDRS, HAMA, Y-BOCS, GAF) before implantation and during the 6-month follow-up period, including stimulation parameters and values before the neurostimulation (START) and after cessation of the neurostimulation – OFF

HDRS – Hamilton Depression Rating Scale; HAMA – Hamilton Anxiety Rating Scale; Y-BOCS – Yale-Brown Obsessive-Compulsive Scale; GAF – Global Assessment of Functioning

6.3. Control appointments

A clinical efficacy evaluation was carried out according to predetermined time frames. During the first control visit, the patient reported a feeling of general well-being with respect to the surgical procedure, but with no improvement in psychopathological symptoms. In the psychometric evaluation, the results of the Y-BOCS and SOFAS were analogous to the results obtained before the procedure – 28 points and 45 points respectively, however, there was a deterioration in the symptoms of his anxiety score, measured using the HAMA scale (from 6 points before the start of stimulation to 11 points), and depressive symptoms, measured using the HDRS (from 7 points before stimulation to 14 points).

However, an improvement in psychopathological symptoms was seen during the following control appointment. According to the patient's reports, he experienced a reduction in the number and frequency of compulsive activities, as well as activities carried out in order to mitigate obsessive thoughts, as well as the need to repeat said activities. There was a reduction in all three symptom categories in relation to the initial assessment: to 18 points on the Y-BOCS (reduction of 36%); to 10 points on the HAMA scale (reduction of 29%) and to 7 points on the HDRS (reduction of 36%). The SOFAS score remained at 45 points (no significant improvement in general functioning and activity was observed). The improvements reported by the patient persisted into the following weeks, a further reduction in OCD symptoms (Y-BOCS after 5 weeks – 15 points) and anxiety symptoms (HAMA – 6 points) was observed as well as improvement in overall functioning (SOFAS after 5 weeks – 50 points), however, without changes in depressive symptoms (HDRS – 7 points).

The patient began to undertake more everyday household activities, managing to refrain from 'deferring', he was more and more willing to leave his apartment, he expressed satisfaction with the improvement he observed. After two weeks, the patient complained of a deterioration in his mental state, he noticed a reduced ability to control his compulsions, an increase in their frequency and a secondary decline in overall activity. Deterioration was recorded over all measured categories, including the Y-BOCS score – with an increase to 21 points, SOFAS – a decrease to his initial score of 45 points, an increase in his HAMA score to 14 points and in the HDRS score to 10 points. It was then decided to modify the stimulation parameters, increasing the voltage from 3 V to 3.5 V. This modification resulted in the return to the previously observed improvements – the patient's condition over the following weeks, until the stimulation was halted, remained fairly stable (Y-BOCS in the range of 12–16 points and SOFAS at 50 points, HAMA from 0 to 6 points and HDRS from 4 to 6 points).

Despite the improvement, the patient did not undertake any form of employment, attributing it to his persistent symptoms of social anxiety. During the follow-up appointments no changes were made to his pharmacotherapy.

6.4. CBT psychotherapy

Due to the fact that at the time of the study he was already undergoing individual cognitive behavioral therapy for a year, he remained with his current therapist. In the absence of more objective (derived from the therapist) data in relation to the patients' therapy, the description of the therapy sessions is based on accounts from the patient himself. According to the patient's description, the therapeutic process in which he participated was similar to that of the first case study. He performed home exercises such as exposure to anxiety inducing stimuli related to the content of his obsessive thoughts, this had no significant effect on the reduction of his symptoms. As a result of the high level of anxiety associated with his obsessions related to religious and blasphemous content, the patient had considerable difficulty in undertaking exposure exercises and tasks related to these obsessions. Similarly, to patient 1, after switching on the stimulation, the patient was more willing to undertake exposure assignments, which were aimed at reducing compulsions while also completing them with greater ease, at home, however, the total number of obsessions reduced only slightly. Similarly to patient 1, patient 2 eventually discontinued the therapy in April 2018 (about 4 months after turning on the stimulation).

6.5. Attempt to turn off the neurostimulator

As in the previous case study, at the end of the observation period, a blind test was undertaken to switch off the neurostimulator, while maintaining the same procedure. The patient observed a change in mental state 3 days after turning off the neurostimulation. What prevailed over a short period of time was a loss of control over his compulsions, an intensification of the need to control his obsessive thoughts as well as the frequency of said thoughts. At this time the patient withdrew from his daily activities. The peak intensity of the symptoms occurred one week after switching off the neurostimulation, after which it stabilized, however, the intensity of the aforementioned symptoms was lesser than before implantation of the neurostimulator. Two weeks after switching off the stimulation, the Y-BOCS score increased to 19 points (a reduction of 32% compared to the pre-implantation score), the SOFAS score decreased to 45 points (no change in relation to the pre-implantation score), and slight increase in symptoms on the HAMA scales (7 points – an increase of 17% compared to pre-implantation) and HDRS score (7 points – analogous to pre-implantation) was observed (Figure 2: IX evaluation 'OFF'). Resuming the neurostimulation resulted in a return to the previously obtained improvements in symptoms (Y-BOCS – 12 points, SOFAS – 50 points, HAMA – 6 points, HDRS – 4 points) (Figure 2: X evaluation). The patient's mental state remained relatively stable until the end of the 6-month observation period.

7. Conclusions and discussion

The results obtained in both cases show the effectiveness of DBS in the reduction of obsessive-compulsive symptoms. Neurosurgical intervention was accepted and well tolerated by patients and proceeded without side effects, which corresponds to the experiences of patients from other studies [21]. In both patients who underwent the surgery, there were differences in improvement and subsequent regression of symptoms after switching off the stimulation. The first patient showed a reduction of 43% in the Y-BOCS score after the six-month follow up period, while in patient 2 there was a reduction of 64%. In both cases at the end of the follow-up period a slight decrease in depressive symptoms was noted. In patient 1, there was a slight reduction in the HDRS score – of 13%, while in patient 2 there was a reduction of 33%. There was a slight difference between the two patients in the HAMA scale: patient 1 – a reduction of 2 points, and patient 2 – an increase of 2 points. This was similar to a study conducted by Fayad et al. [22] which showed a general decrease in the severity of OCD symptoms, measured using the Y-BOCS questionnaire, with a noticeable fluctuation of symptoms over the individual measurement points. In this study an increase in the severity of depressive symptoms in relation to the baseline level was noted. The authors point to life circumstances here as the probable cause of changes in depressive symptoms, while stressing that the study group is at high risk of developing depression. In contrast, the deterioration in the severity of anxiety symptoms observed in patient 2 is associated with co-morbid social anxiety.

The patients' mental state was carefully evaluated for potential DBS side effects on every appointment. No manic or hypomanic symptoms were observed. No psychometric tools were used to detect the severity of such symptoms. The researchers decided to include the aforementioned tools in future studies because the elevated mood is commonly reported as a side-effect of DBS in various neuroanatomical locations [23].

Similarities between the two cases can also be seen with regards to initial levels of functioning (pre-DBS), these include: the early onset of symptoms, low level of daily activity, including a lack of regular work and low level of social functioning. The differences are related to gender, the level of insight into the cause of their symptoms and the severity of OCD symptoms (35 and 28 points in the Y-BOCS, respectively). In the meta-analysis regarding the effectiveness of DBS and predictors of a positive response to treatment, conducted by Alonso et al. [19], no significant differences between the genders and the effectiveness of DBS were found. Differences in the reduction of symptoms in the presented cases are probably the result of the initial levels of symptom severity.

In the study by de Haan et al. [24], patients reported the subjective effectiveness of DBS interventions in the form of greater ease of involvement in tasks defined in their respective CBT course. Low involvement in therapy in both of the presented cases is in contradiction to data obtained by other authors. The differences in the presented data

may be due to how the concept of involvement in therapy is defined. The greater ease of performing the tasks by the patient during the therapy does not have to be associated with the general motivation to undertake or continue psychotherapeutic treatment. Patient 1 showed low motivation from the very beginning of therapy. Greater ease of engaging in tasks obtained through the use of neurostimulation may not have been enough to build motivation for psychotherapeutic treatment.

In the study by Mantione et al. [9], the original therapeutic protocol was modified to accommodate DBS patients. The authors pay special attention to the motivation needed to undertake therapy (reduction of symptoms), including expectations regarding therapy and life without symptoms. In addition, the authors describe the phenomenon they observed, whereby patients tend to ignore the positive effects of the procedure and focus their attention on the symptoms that have not yet subsided. This effect could also be observed in the patients described above. The proposed modifications of the therapeutic protocol include the introduction of additional interventions aimed at reducing negative beliefs about therapy, strengthening motivation by drawing the patient's attention to the positive changes achieved through the DBS. Following the assumption of researchers that CBT reduces compulsive symptoms with an adequate (allowing exposure) level of anxiety [9], in future cases it would be necessary to check whether the subsequent introduction of CBT (after further improvement of symptoms, especially in terms of anxiety reduction) would not be of greater benefit. Especially, taking into account the consequences of inappropriate interventions, which further reinforce the negative attitude of the patient towards therapy and potentially reduce the motivation to undertake any attempts to fight the symptoms.

In both cases, after cessation of the stimulation, there was a deterioration of OCD symptoms, albeit with differing dynamics between patients. Patient 1 experienced an increase in symptoms within less than one hour of turning off the neurostimulator. Patient 2 reported worsening a few days after turning off the stimulation. A similar dynamics was observed when switching on stimulation – patient 1 reported improvement after a much shorter time than patient 2 (a difference of a few days). Recurrence of symptoms after cessation of the stimulation, recorded in patient 1, clearly shows the relationship between the severity of symptoms and DBS stimulation. In the case of patient 2, the improvement was more persistent and less dependent on stimulation, however, a gradual deterioration in the severity of symptoms was observed. The presented data suggest that DBS effectively reduces OCD symptoms.

In the presented cases it is important to note that after cessation of OCD symptoms secondary issues began to arise. The authors of the work on biographical disruption indicate the biographical significance of the DBS procedure by introducing the concept of 'burden of normality' [25]. Many years of life with an illness that affects all areas of functioning and a sudden resolution of symptoms, as a result of neurosurgical intervention, requires adaptation to a life free from said disruptions. In the case of both patients,

despite a significant reduction in OCD symptoms, there was no significant improvement in the functioning of objective indicators (work, home duties, interpersonal relations). Previously, patients associated deficits in their functioning with OCD symptoms.

It should be mentioned that with further observation one can expect a progressive improvement in overall functioning. Similar dynamics, i.e., reduction of OCD symptoms without a satisfactory change in social and environmental performance in the first months after the start of stimulation, corresponds to the reports of other researchers [26].

Recapitulation

1. The pilot study confirms that there is a group of OCD patients resistant to standard treatment regimens that may benefit from DBS.
2. The improvement observed after the use of DBS with concomitant pharmacotherapy and psychotherapy can be significant, however, this is in large part dependent on the patient's personality, family support network and home environment.
3. There is a need for further multicenter studies on the use of DBS in OCD and other psychiatric disorders refractory to treatment in order to formulate appropriate criteria for the qualification of patients and to find the best neuroanatomical sites in the brain for optimal stimulation.

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