# DEEP BRAIN STIMULATION FOR TREATMENT REFRACTORY OBSESSIVE-COMPULSIVE DISORDER – A CASE REPORT

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**TERÁPIAREZISZTENS KÉNYSZERBETEG KEZELÉSE MÉLY AGYI STIMULÁCIÓVAL – ESETISMERTETÉS**
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In the last 30 years it has been a great development in the understanding and therapy of obsessive-compulsive disorder. Adequate pharmaco- and cognitive-behavior therapies reduce the symptoms in 40-60% of patients, so a remarkable portion of patients still remains refractory to conventional treatment. Neurosurgery – with it's reversible and irreversible techniques – brought a breakthrough in the therapy of treatment refractory patients. In the present case, we represent a 3 months follow-up of an obsessive-compulsive patient treated by deep brain stimulation. In our case, the stimulation target was the anterior limb of internal capsule. The clinical symptoms were measured by Y-BOCS. In addition various neuropsychological tests were used to monitor patient's executive functions before and 3 months after the deep brain stimulation. We found that obsessive-compulsive symptoms improved after three months of the stimulation. The neuropsychological tests showed improvement in some executive functions (e.g. fluency, set-shifting, decision making). On the other hand our results revealed severe neurocognitive – mainly attention skill – deficits in a treatment refractory obsessive-compulsive patient.

***Keywords:*** *treatment refractory obsessive-compulsive disorder, deep brain stimulation, neuropsychology, executive functions*

Az utóbbi 30 évben jelentős fejlődés történt a kényszerbetegség mechanizmusának megértésében és terápiájában. Az adekvát farmako- és kognitív viselkedésterápia alkalmazása mellett a betegek közel 40-60%-a javul, ugyanakkor a betegek egy része terápiarezisztensnek tekinthető. A terápiarezisztens betegek kezelésében áttörést jelentett az idegsebészeti eljárások megjelenése. Az idegsebészeti eljárások közé irreverzíbilis és reverzíbilis beavatkozások tartoznak. Esetismertetésünkben mély agyi stimulációval kezelt kényszerbeteg három hónapos követésének eredményeit mutatjuk be. A capsula interna anterior ágán történt a mély agyi stimuláció. A beteggel a beavatkozás előtt és után három hónappal klinikai tüneteket mérő skálát (Y-BOCS) és végrehajtó funkciókat vizsgáló neuropszichológiai teszteket vettünk fel. Eredményeink szerint a kényszeres tünetek a mély agyi stimulációt követő három hónapban javultak. A neuropszichológiai tesztek egyes végrehajtó funkciók (fluencia, szempontváltás, döntéshozás) javulását jelezték, ugyanakkor az eredményekből kirajzolódik a terápiarezisztens kényszerbetegekre jellemző neurokognitív – elsősorban a figyelmi képességek – súlyos deficitje is.

***Kulcsszavak:*** *terápiarezisztens kényszerbetegség, mély agyi stimuláció, neuropszichológia, végrehajtó funkciók*

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Obsessive-compulsive disorder (OCD) is characterized by anxiety-provoking intrusive thoughts (obsessions), mainly leading to compulsive behaviors or mental rituals to temporarily decrease the anxiety provoked by the obsessions. Symptoms generally begin in childhood and adolescence and often result in severe impairments in social and occupational functioning[1].

There has been remarkable development in the understanding of the underlying mechanism of OCD over the last 30 years. Despite the growing number of treatment options available, nearly 40% of OCD patients do not respond well to adequate therapeutic methods[2]. These patients are considered treatment-refractory patients.

Neurosurgical methods brought a breakthrough in managing treatment-refractory OCD patients[3]. The neurosurgical methods cannot be understood without the most recent biological theories of OCD, namely the loop theories. The loop theories[4–7]

describe the connections and interactions between neuro-anatomical structures involved in OCD, and have been developed on the basis of neuro-imaging findings, like structural (CT or MRI)[8, 9] and functional (fMRI)[10] abnormalities in brain regions. In addition, an increasing amount of data is available on cognitive deficits in OCD patients from the late 1990s[11–14]. The most recent studies[15–19] combine functional neuro-imaging techniques with neuropsychological tasks by imaging brain functions during cognitive testing in order to objectify the activity of given brain areas. In our opinion, in addition to functional imaging and cognitive tests, neurosurgical methods also can provide insight into the function of loops.

Most neurosurgical techniques try to influence the connections between cortical areas (e.g., orbitofrontal cortex, cingulum), basal ganglia (mainly caudate nucleus), and medial dorsal thalamic nucleus. OCD symptoms occur, when there is an abnormal positive feedback in the orbito-fronto-thalamic circuit, inadequately inhibited by the cortex-striatum-thalamus-cortex loop (CSTC), in other words the CSTC loop is hypoactive, when orbito-fronto-thalamic loop is hyperactive[1].

Surgical interventions at certain locations of neuronal pathways have consequential effects on the whole network, therefore they may influence symptom severity. Irreversible (e.g., cingulotomy, subcaudate tractotomy, limbic leucotomy, anterior capsulotomy) and reversible (e.g., deep brain stimulation – DBS) surgical techniques were developed to treat patients with OCD.

Below, we summarize the results of previous studies about the use of DBS in OCD (**Table 1.**).

In the late 1990's Nuttin et al. published the first case series of four patients with treatment-resistant OCD undergoing DBS. Authors reported that DBS had beneficial effects in OCD[20].

In almost all reported cases, a bilateral stimulation was applied in the anterior limb of the internal capsule, similar to the target region of the anterior capsulotomy. The benefit of this method is the reversibility, in contrast to the irreversible neurosurgical methods. Case studies have verified the success of DBS[21].

Gabriels et al. investigated the efficacy of DBS in three OCD patients. In their opinion, the stimulation of the anterior limbs of the internal capsules, is a possible alternative of anterior capsulotomy. Accordingly, they suggested that the stimulation should precede the irreversible capsulotomy. They reported that the symptoms of two patients improved. In case of one patient they processed anterior capsulotomy after a year of unsuccessful stimulation; the anterior capsulotomy was associated with a more pronounced symptom improvement than the DBS. Assessed with neuropsychological measures, authors found, that DBS does not cause global cognitive deficits (but all patients showed perseverative errors in Wisconsin Card Sorting Test[22]). On the contrary, they found improvements in IQ scores and memory functions.

Abelson et al. examined the effects of DBS for treatment-refractory OCD in four patients, with leads placed bilaterally in the anterior limbs of the internal capsule. During the 3-weeks stimulation blocks one patient showed a greater than 35% improvement in OCD symptoms, while one patient showed a moderate benefit. According to Abelson et al., these improvements are comparable to those achieved with ablative anterior capsulotomy. The tests for attention, working memory, and verbal fluency were administrated before and 3 weeks after the DBS. Authors did not experience consistent changes in cognitive patterns of their patients: the mental flexibility (Stroop interference) improved in two patients, while it worsened in one. Verbal fluency worsened in one case. One of their four patients committed suicide after one year of the beginning of stimulation; authors explained this serious adverse event by depressive relapse[23].

Beyond the internal capsule, there are more promising targets of deep brain stimulations in the treatment of OCD. Tass et al. suggested the electrical stimulation of the nucleus accumbens – where the stimulation influences the internal capsule-nucleus accumbens-limbic structures-amygdala-basal ganglia-thalamus-orbito-frontal region loop – in the treatment of treatment-refractory OCD[24]. The nucleus accumbens is important in information screening as it was proved by the consequences of subcaudate tractotomy.

Huff et al. investigated the effects of stimulation of nucleus accumbens. They also considered, the nucleus accumbens as a promising target for DBS, because of it's predominant role in the modulation of the activity of cortico-striato-thalamo-cortical circuits. They supposed that the stimulation of the nucleus accumbens would have an additional effect on the internal capsule. The study was designed as double-blind and "placebo" (shame stimulation) controlled. The clinical symptoms improved significantly, but authors did not find significant changes in anxiety and cognitive functions[25].

Okun et al. also gave their attention to the nucleus accumbens. In their study the electrodes were placed in the region of the right anterior limb of the internal capsule and into the centre of the nucleus accumbens. Authors have applied both "shame" and "effective" deep brain stimulations in their study. They found that clinical symptoms improved

**Table 1.** *Studies about deep brain stimulations*

| Author | Number of patients | Diagnosis | Target of deep brain stimulation | Follow-up | Tests | Results |
|---|---|---|---|---|---|---|
| Nuttin, 1999 | 4 | OCD | anterior limbs of internal capsules | | | clinical improvement |
| Gabriels, 2003 | 3 | OCD | anterior limbs of internal capsules | 1 year | Raven WCST PASAT CFR Digit Span Test VFT ToL | clinical improvement IQ, memory improved perseveration |
| Anderson, 2003 | 1 | OCD | anterior limbs of internal capsules | 10 months | Y-BOCS | clinical improvement |
| Abelson, 2005 | 4 | OCD | anterior limbs of internal capsules | 3 weeks | Y-BOCS Corsi Block Span, Digit Span, Stroop Test, VFT | clinical improvement in two patients no cognitive changes |
| Tass, 2003 | 3 | OCD | nucleus accumbens | 15 months | Y-BOCS | clinical improvement in two cases |
| Okun, 2007 | 5 | OCD | anterior limbs of internal capsules, nucleus accumbens | 1 months | – | – |
| Huff, 2009 | 10 | OCD | nucleus accumbens | 12 months | Y-BOCS VFT ToL CPT | clinical improvement No cognitive improvement |
| Aouizerate, 2004 | 1 | OCD | ventral caudate | 15 months | Y-BOCS, FCSRT, BVRT, TMT WCST Stroop Test, ZCT, IST | clinical improvement visual memory, set shifting improvement |
| Rauch, 2006 | 6 | OCD | ventralcapsule, ventral striatum | 3 months | Y-BOCS | clinical improvement |

Y-BOCS: Yale-Brown Obsessive Compulsive Scale; Raven: Raven Progressive Matrix Test; PASAT: Paced Auditory Selective Attention Test; CFR: Rey-Osterrieth Complex Figure Test; WCST: Wisconsin Card Sorting Test; BVRT: Benton Visual Retention Test; FCSRT: Free and Cued Selective Reminding Test; TMT: Trail Making Test; ZCT: Zazzo Cancellation Task; IST: Isaacs Set Test; VFT: Verbal Fluency Test; ToL: Towers of London Test; CPT: Continuous Performance Test

significantly only during the "effective" (i.e. active) stimulation[26].

Aouizerate et al. published a case study, in which they tested the hypothesis that DBS of the ventral caudate nucleus might be effective in treating intractable OCD[27]. The symptoms of the patient improved, so the role of the caudate nucleus (and the whole striatum) – in accordance with the results of structural and functional neuroimaging studies – has been verified with DBS. There is evidence for the major role of the ventral striatum in the processing of emotional and motivational cortical regulated behaviors, impaired in OCD. The performance was followed-up for 6 months with various neuropsychological tests. The improvement of visual memory performance and the set-shifting performance assessed with the WCST was constant, but the attention functions improved only temporarily.

Rauch et al. verified the efficacy of DBS with PET investigation. He measured the cerebral blood flow during DBS at high and low frequency. During high frequency DBS significant activation of

the orbitofrontal cortex, anterior cingulate cortex, striatum, globus palidus and thalamus was detectable[28]. This investigation verified that during DBS that loop became active, which has an important role in the etiology of OCD.

We present the case of a patient with intractable OCD who was treated with bilateral electrical stimulators that were placed stereotactically in the anterior limbs of the internal capsules.

The aim of our study was to investigate how modify this kind of stimulation the severity of obsessive-compulsive symptoms and executive functions.

## Method

### ENTRY CRITERIA

Our patient had treatment-refractory OCD. We define treatment-refractory OCD patients as those who undergo adequate number of with SSRIs (minimum 3 types of SSRI at maximum dosage for at least 12 weeks), standard augmentation strategies (consecutive administration of two atypical antipsychotics) and behavior therapy (minimum duration: 30 hours) without satisfactory treatment response[29]. Entry criteria included Y-BOCS score at least 25; no history of psychotic disorder; no current substance use disorder. The patient gave informed consent prior to surgery.

### SURGICAL PROCEDURE

After presurgery investigation – including MRI examination – KINETRA type double neuropacemaker was implanted. The target coordinates and entries at both sides were determined by a computer program. A leading angle of the electrodes was 85° sagittal and 65° coronal, and targets were determined at anterior limbs of internal capsule in both sides. On both sides the neurosurgeon made a 14 mm frontal bore, then the TCU002 electrode was led into the target. The electrodes (DBS lead kit model 3389) were led and fixed to the skull-bone. On the right side a skin pocket was made for the pacemaker; the connectings were joined to the brain electrode. The other end of connectings was joined to the KINETRA type double neuropacemaker (Medtronic Extension kit 7482). The pacemaker was started on 2.0 V base-value, the upper value was limited on 2.8 V on both sides. No adverse events occurred during the surgical procedure.

### MEASURES

Pre-stimulation examinations included structural imaging (MRI) and detailed neuropsychological tests [Verbal Fluency Test (VFT), Category Fluency Test (CFT), Trail Making Test (TMT), California Sorting Test (CST), Iowa Gambling Test (IGT), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)]. These tests measure executive functions, namely attention, flexibility, memory, set-shifting, decision making, problem-solving. Eliminating the learning effects, we used alternative versions of the same tests, if it was possible (RBANS, Iowa Gambling Test); in cases of other tests – which have no alternative versions – we had to be satisfied with the 3 months period between the two measure points. We used the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Y-BOCS-SRS (Self Rating Scales) to assess obsessive-compulsive symptoms and the State-Trait Anxiety Inventory (STAI) to identify anxiety symptoms. Pre-stimulation examination was carried out one month before the stimulation. Post-stimulation examinations were performed in the fourth month after the beginning of the stimulation.

## Results

### PRESENTATION OF THE CASE

The 37 years old patient with treatment-refractory OCD has been treated from age 17 years and he was hospitalized several times. He has many different obsessions and compulsions. His main symptoms are intrusive aggressive and contamination thoughts, washing and checking compulsions. His main fear was to harm somebody. Because of the symptoms he was totally disabled, he lost his job, and isolated totally. The obsessive-compulsive symptoms were present every day, he was not able to leave his flat unaided for years and he needed his parents' permanent help in every aspect of his life. In months before the stimulation, he spent his days in his bed, because of his fears, about his possible harmful behavior. Associated with his obsessions, he made complex checking rituals. Our patient had no history of previous suicide attempt(s) or psychosis. He was aware of his illness. The medical history of his family was positive for anxiety disorders: his brother suffers from generalized anxiety disorder.

In our case, combined pharmaco- (antidepressants, anxiolytics and antipsychotics) and psycho- (behavior, family and psychodynamic therapy) therapies were ineffective.

In the monitored three months period after the DBS we experienced a significant improvement in patient's quality of life. He moved back to his own flat, and did not need a permanent support from his parents. The medication was changed: we reduced

the dose of anxiolytics and discontinued the administration of antipsychotics. Only the antidepressant therapy remained unchanged. Our patient reported reduced OCD symptoms; his checking rituals decreased, the obsessions-free periods were longer, and he had more spontaneous actions. He was not yet able to walk alone, but he accepted help from a nurse, who regularly visited him at home. Patient began a behavior therapy again.

CLINICAL AND NEUROPSYCHOLOGICAL CHANGES

**Table 2** shows changes in clinical status and changes in neuropsychological performance.

Changes in clinical condition were measured by Y-BOCS and STAI. The patient showed post-stimulation improvement in obsessive-compulsive and anxiety symptoms as well. The self reported and clinicians scored Y-BOCS decreased with 14 scores; the self-reported Y-BOCS changes mean 35% improvement. Significant improvement was found in STAI scores as well; both state and trait anxiety improved significantly after the beginning of the stimulation.

Changes in the patient neuropsychological profile were measured by the neuropsychological test battery mentioned above. Four tests showed improvement, while two tests showed deterioration. We found improvement in Verbal Fluency and Category Fluency Test; the patient found more words and categories after beginning the stimulation, then before the stimulation. The patient found more right concept in the California A Sorting Test. In the Iowa Gambling Test patient selected fewer cards from the disadvantageous desks, while he chose more from the advantageous desks. We found decreased performance in the Trail Making B test, and in the RBANS Language Index, Attention Index and Visuospatial-Constructional Index.

The performance of the patient in the RBANS Attention and Delayed Memory trials was quite poor both before and after the stimulation.

**Table 2.** *Clinical and neuropsychological changes*

| Test name | Baseline | After DBS | Changes |
|---|---|---|---|
| Y-BOCS | 32 | 18 | +44% |
| Y-BOCS-B | 40 | 26 | +35% |
| STAI-S | 54 | 38 | +30% |
| STAI-T | 65 | 44 | +32% |
| Verbal fluency | 41 | 49 | +16% |
| Perseveration | 2 | 2 | 0% |
| Category fluency | 48 | 56 | +14% |
| Perseveration | 2 | 1 | –50% |
| Intrusive errors | 2 | 3 | +34% |
| California-A | | | |
| Right concept | 4 | 9 | +56% |
| Wrong concept | 1 | | |
| Perseveration | 1 | | |
| California-B | | | |
| Right concept | 5 | 5 | 0% |
| Wrong concept | 2 | 2 | 0% |
| Perseveration | 1 | | |
| Trail Making-A | 40sec | 31sec | +23% |
| Trail Making-B | 68sec | 89sec | –24% |
| Gambling | 47/53 | 37/63 | |
| RBANS | | | |
| Immediate memory | 76 | 81 | +6% |
| Visuospatial-constructional index | 109 | 92 | –16% |
| Language index | 92 | 74 | –20% |
| Attention index | 64 | 56 | –13% |
| Delayed memory | 56 | 56 | 0% |

DBS: Deep Brain Stimulation; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale; STAI: State-Trait Anxiety Inventory; Gambling: Iowa Gambling Test; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status

## Discussion

Deep brain stimulation is a potential method in the treatment of treatment-refractory OCD. Till now the efficacy of DBS is verified only by case reports. Only a few studies compared the cognitive status of patients before and after the DBS.

We have focused on a treatment-refractory patient and his cognitive profile in this case report. Our patient underwent a DBS targeting the anterior limbs of the internal capsules. The treatment was effective and the clinical (obsessive-compulsive and anxiety) symptoms of our patient improved. We did not observe side effects; the procedures and stimulation were well tolerated by the patient. The extent of clinical improvement in our case study is similar to those experienced by Nuttin et al. and Anderson et al. among their patients.

Considering changes in different aspects of neuropsychological performance, our results are mixed. Specific neuropsychological deficits were demonstrated in our case study: the patient had extremely serious attention and memory deficits before stimulation (Attention Index, Delayed Memory Index) and these performance disturbances were unchanged after the stimulation as well. Our findings raised the possibility that attention and memory deficits are characteristic for treatment-refractory patients. This possibility is in contrast with the results of Gabriel et al., who observed memory improvement after DBS.

In our case, certain cognitive performances (category fluency and decision-making) improved after the stimulation.

The results of decision-making related Gambling Test showed that patient has become more sensitive to feedback (i.e., reward and punishment) and has

improved his ability to create strategy. This positive change in the sensitivity to feedback creates favorable conditions for psychotherapy and rehabilitation. In our opinion, the aim of neurosurgical interventions should be to make patients with treatment-refractory OCD suitable for psychotherapy.

We plan to further follow up the patient, regarding his clinical course and cognitive performance.

In conclusion, DBS may be a reversible last resort alternative for patients with treatment-refractory. Our results are promising, but they need to be confirmed by further studies. In our case, DBS reduced OCD symptoms, and improved the patient's quality of life. Psychiatric counseling and neuropsychological examinations remain important after DBS in order to control changes in the clinical symptoms and executive functions as well. In our opinion, DBS may be only a part of a complex treatment strategy, which consists of pharmacotherapy, psychotherapy, and possible psychosurgery.

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