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Deep brain stimulation: new possibilities for the treatment of mental disorders

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Summary

Deep brain stimulation (DBS) is a treatment method that is currently getting more and more attention from psychiatrists. It has proven to be efficacious and safe in the treatment of neurological disorders, mainly Parkinson's disease (PD), dystonia and essential tremor. DBS has very often contributed to successful treatment in cases that had proved resistant to all other methods of treatment.

Nowadays treatment-resistant obsessive-compulsive disorder (OCD) is the main psychiatric indication for DBS. Many studies have focused on assessing the efficacy and safety of this method in different mental disorders, including depressive disorders, Alzheimer's disease, anorexia nervosa, Tourette syndrome, substance addiction or aggressive behaviors. Single cases of successful treatment in bipolar disorder, schizophrenia and post traumatic stress disorder have also emerged in recent years. In this review the current state of knowledge on the applicability of DBS in psychiatry is presented, based on the available systematic reviews, clinical trials and case studies, as well as on neurophysiological and neuroimaging data.

Key words: deep brain stimulation, treatment-resistant mental disorder, neuromodulation

Introduction

The first use of chronic deep brain stimulation in the treatment of neurological disorders was documented in 1963 by Natalia Petrovna Bekthereva, a neurobiologist at the Institute of Experimental Medicine and the Academy of Medical Sciences in Leningrad [1]. The first long-term high-frequency stimulation, replacing short-term stimulation with subsequent ablation in the treatment of movement disorders, was described by Benabid et al. in 1987 [2]. The safety and efficacy of DBS as a ther-

apeutic method were established on the basis of its success in treating movement disorders [3, 4].

In 1997, the US Food and Drug Administration (FDA) approved thalamic DBS for essential tremor and PD-related tremor. In 2003, the FDA approved the use of DBS devices for stimulation of the subthalamic nucleus (STN) and internal globus pallidus (Latin: *globus pallidus internus* – GPi) in PD patients, and for the treatment of primary generalized and segmental dystonia. Approval for the use of DBS in obsessive-compulsive disorder was given in 2009 [5].

In the next three chapters of this review, we present current knowledge on the three most broadly described mental disorders treated with DBS (OCD, major depressive disorder and Tourette syndrome). Further sections of the review focus on more experimental indications.

1. Obsessive-compulsive disorder (OCD)

DBS has been proposed as a treatment option for patients with treatment-resistant obsessive-compulsive disorder. The highest number of surgical procedures has been performed in this particular group, among all mental disorders, and efficacy of this treatment is well documented. In recent years, many different brain regions have been suggested as possible targets for stimulation in OCD patients. The first target of OCD treatment was the anterior limb of the internal capsule (ALIC), as described by Nuttin et al. [6]. Since then, other possible targets have been proposed in the literature. Striatal targets include the nucleus accumbens (NAc), ventral capsule/ventral striatum (VC/VS) and ventral area of the caudate nucleus [7]. Another possible target is the subthalamic nucleus (STN) [7]. In 2009,, the FDA granted permission for ALIC-DBS under the Humanitarian Device Exemption [8]. Two years later European authorities gave the CE marking to ALIC-DBS for severe OCD. Recent years have brought propositions of new targets: the bed nucleus of the stria terminalis (BNST), the inferior thalamic peduncle (ITP) and the superior lateral branch of the medial forebrain bundle (MFB) [9].

2.1. Stimulation targets and efficacy

A broad systematic review with a meta-analysis comparing the effects of ALIC and STN stimulation failed to show any significant differences between these two targets in terms of the effects of the treatment. However, a total of 60% of DBS patients were classified as responders –with response defined as a reduction of at least 35% in their scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and an average decrease of approx. 45% in Y-BOCS scores was observed [10]. The same meta-analysis also showed that older age at OCD onset is a predictive factor for DBS response, while the duration of OCD symptoms before DBS implantation does not differ between responders and non-responders. Also, responders more frequently reported OCD symptoms with religious or sexual content than non-responders [10].

Another interesting study showed that intraoperative smiles and laughter during test stimulation of the ALIC and NAc may be predictive factors for long-term response in OCD patients [11].

The most important functional brain region involved in OCD pathogenesis is called the cortico-striato-thalamo-cortical circuit. Physiologically, cortex activity is passed to the striatum and NAc, from where it is transmitted to the GPi via two pathways: a direct (inhibitory) pathway, and an indirect (excitatory) pathway through the external part of the globus pallidus (Latin: *globus pallidus externus* – GPe) and STN. Subsequently, the GPi inhibits thalamic activity, which is passed to the cortex. Furthermore, striatum and NAc activity is also modulated by the BNST (which also gets excitatory stimuli from the cortex). In healthy patients both pathways remain in balance, while in OCD patients the direct pathway is potentially hyperactive, which might be mediated by BNST. This hyperactivity causes strong inhibition of GPi activity, leading to hyperactive positive feedback of the orbitofrontal cortex [9]. Insufficient striatal control of thalamic activity leads to hyperactivity of the orbitrofrontal cortex (which evokes obsessions) and the anterior part of the cingulate gyrus (which triggers anxiety) [12]. Thus, neuromodulation of different areas of grey and white matter in this circuit could lead to correction of the distorted balance.

The STN was originally a stimulation target for Parkinson's disease. But interest in this particular brain area increased after case reports describing PD patients with comorbid OCD who showed improvement in the symptom severity of both disorders [13, 14]. This positive effect on OCD symptoms was later confirmed in larger studies, summarized in the aforementioned systematic review by Alonso et al. [10]. Mulders et al. [15] summarized clinical and electrophysiological studies on the STN, coming to a conclusion that the STN is responsible not only for motor functions, but also for cognitive and emotional functioning, modulating decision-making and action-selection processes. Having direct connections to the motor, limbic and associative circuits, it processes different stimuli to determine behavioral reactions. The authors also refer to several studies showing STN hyperactivity in OCD, theorizing that the non-motor part of the STN is unable to inhibit unwanted behavioral reactions in OCD patients [15]. The similar response rates of OCD to DBS in the STN and the ALIC may confirm that these regions are parts of the same pathological circuit. However, while DBS in striatal areas (the ALIC and NAc) often leads to a rapid reduction in depressive and anxiety symptoms, this effect is not observed during STN stimulation [10].

Regarding the BNST, ITP and MFB, recent studies suggest that they are very promising targets for DBS in OCD, although the relatively small size of the included groups and a lack of larger controlled studies mean that we must still regard these brain regions as experimental targets [16–19]. Some attention has also been paid to enhancing DBS treatment by introducing post-operative cognitive behavioral therapy (CBT). Although most patients are unable to undergo CBT before DBS treatment, or it is unsuccessful, many patients report that during stimulation they manage to engage in CBT tasks, and they present even greater reduction in OCD symptoms [20, 21].

2.2. Indications, inclusion and exclusion criteria

The most commonly used inclusion criteria for DBS in OCD are as follows:

- Resistance to previous treatment (a lack of or insufficient effect): two courses of SSRI treatment at the maximum dosage for at least 12 weeks; one course of clomipramine treatment at the maximum dose for at least 12 weeks; one adjuvant therapy with second-generation antipsychotic for at least 8 weeks; one course of CBT – at least 16 therapeutic sessions.
- A diagnosis of OCD confirmed in accordance with DSM-5 criteria; a Y-BOCS score of at least 28 points; a GAF score of less than 45 points; OCD duration of at least five years.
- Age between 18 and 65 years.
- An IQ over 80.

Exclusion criteria include:

- Comorbidities: mental disorders (psychotic disorders, bipolar disorder, autism, severe personality disorders, psychoactive substance addiction, dementia), an unstable somatic state, disorders of the CNS (including epilepsy, PD, multiple sclerosis).
- Pregnancy [12, 22].

2.3. Future directions

Reports of elevated mood or even hypomania are present in many studies involving ALIC/NAc stimulation [10]. It has recently been proposed that the introduction of an adaptive DBS (aDBS) system should be considered. A prototype of such a system is currently being developed. In tests, the aDBS system was able to monitor local field potentials during DBS treatment and could adjust stimulation parameters to further reduce obsessive ideations and compulsive behaviors, as well as reduce the risk of side effects in the form of acute mood changes, including hypomania. The use of an automated facial recognition program will contribute to fast recognition of mood changes [23].

The Fifth Annual DBS Think Tank has also proposed that patients could benefit from pre-operative diffusion tensor imaging (DTI) of the ALIC, as recent studies have confirmed that this brain area is highly variable, and DTI during the pre-operative stage could personalize the treatment [23]. Future studies should also include comparisons of the efficacy of DBS in different targets, possibly in controlled trials. For now we can hypothesize that the choice of target could be personalized on the basis of the clinical image – e.g., ALIC/NAc stimulation could be used in patients with high levels of anxiety, while STN stimulation could be preferred in patients with strong stereotypical compulsions [9].

3. Major depressive disorder (MDD)

Etiology of MDD is associated with over-activity in limbic-cortical areas of the brain. It has been noticed that DBS can inhibit excessive stimulation and normalize the activity of limbic-cortical connections, which is thought to provide resolution of MDD symptoms [24].

3.1. Stimulation targets

The VC/VS is the most investigated target of DBS for obsessive-compulsive disorder, MDD and addiction [25]. It has been used as a target in MDD patients as a consequence of DBS of the internal capsule in OCD patients. During DBS trials with OCD patients, mood improvement was noticed before the reduction of OCD symptoms [26]. Studies indicate that the VC/VS and NAc affect the fronto-limbic area. Therefore, trials using DBS in patients with MDD have been carried out extensively [27, 28].

The subcallosal cingulate gyrus (SCG) plays an important role in the pathophysiology of MDD. The SCG has a numerous connections with brain regions that are involved in the evolution of MDD symptoms. Thus direct stimulation of the SCG could affect depressive symptoms [29–31].

The medial forebrain bundle (MFB) is part of the reward system, which connects the NAc, the ventral tegmental area, the amygdala, and the ventromedial and lateral nuclei of the hypothalamus. The reward system has recently been investigated regarding its impact on motivated behavior, which is disturbed in depressed patients [32, 33].

The NAc also fulfills a key function in the reward circuitry [34]. Dysfunction in the NAc regarding rewarding stimuli has been observed in MDD patients [35]. Moreover, studies have shown that DBS of NAc alters the levels of monoamines in the prefrontal cortex (PFC) [36].

3.2. Efficacy

The effects of DBS as a treatment for MDD are not as spectacular as originally expected. A lot of open-label studies have shown decreases in depressive symptoms after stimulation of various targets, such as the VC/VS, SCG, MFB and NAc [33, 37–40]. However, double-blinded trials have not been as encouraging. Indeed, depressive symptoms decreased significantly in most studies, but no significant differences between sham and active stimulation was observed. Two large randomized double-blind and sponsored studies were recently conducted. One of them involved stimulation of the VC/VS; it was supposed to include 200 patients, but was finished after 29 patients because of a lack of significant difference between sham and active stimulation [27]. A similar situation was observed in the largest study of DBS for depression; it included 90 patients and targeted the SCG. 30 patients received sham stimulation and 60 active stimulation; there was no significant difference between those groups [30].

However, researchers are still looking for the optimal stimulation target, and there are many options that have yet to be investigated. For example, the MFB is a very promising target for DBS in MDD – a pilot study performed by Schlaepfer et al. [33] showed a significant decrease in *Montgomery-Asberg Depression Rating Scale* (MADRS) scores after only seven days of stimulation. After 33 weeks, six out of seven patients were classified as responders [33]. Another study that targeted the MFB produced consistent results: It was single-blind study in which the patients had sham stimulation for four weeks, after which active stimulation was turned on and the patients were unblinded. There was a significant decrease in MADRS scores during the sham period, although the authors thought it could be associated with inflammation or neurotransmitters released due to the insertion of the neurostimulators [32]. Further studies must definitely be done regarding potential stimulation of the MFB.

The NAc is another DBS target that has not been fully examined. A study that was not sham-controlled showed a significant decrease in depressive symptoms, an anti-anhedonic effect and also an anti-anxiety effect, which was not noted in other studies [37].

3.3. Indications, inclusion and exclusion criteria

Commonly used inclusion criteria for DBS in MDD are as follows:

- Resistance to previous treatment (lack of or insufficient effect): three courses of treatment with antidepressant drugs in adequate doses for at least six weeks – including at least one treatment with a serotonin and norepinephrine reuptake inhibitor (SNRI) or tricyclic antidepressant; adjuvant therapy with lithium or second-generation antipsychotic drug for at least six weeks; at least one course of CBT or interpersonal therapy (at least 16 therapeutic sessions); one course of electroconvulsive therapy or contraindications for this treatment.
- A diagnosis of MDD confirmed in accordance with DSM-5 criteria; a score of at least 20 points on *the Hamilton Depression Rating Scale-17* (HDRS-17) or at least 25 points on *the Montgomery-Asberg Depression Rating Scale* (MADRS); a GAF score of less than 50 points; MDD duration of at least five years.
- Age between 18 and 65 years.
- An IQ over 80.

Exclusion criteria include:

- Comorbidities: mental disorders (psychotic disorders, bipolar disorder, autism, severe personality disorders, psychoactive substance addiction, dementia), an unstable somatic state, disorders of the CNS (including epilepsy, PD, multiple sclerosis).
- Pregnancy.

– The presence of some MDD-related symptoms: auto-aggressive behaviours, self-injuries, suicidal tendencies, a present risk of suicidal acts, unstable and severely impaired functioning [12, 22].

3.4. Conclusions

The use of DBS for patients affected by MDD is very promising, but researchers need to let the initial enthusiasm settle. Most studies have shown no significant difference between active and sham stimulation, although the results − more than 50% improvement in depression scale scores, alterations in neurotransmitter levels and noticeable influence on neuroplasticity − demonstrate that more controlled trials are needed.

4. Tourette syndrome

Tourette syndrome (TS) is a set of symptoms characterized by involuntary motor and vocal tics beginning in childhood. It is often comorbid with obsessive-compulsive disorder and attention deficit hyperactivity disorder [41]. The pathomechanism of involuntary tics consists in impairment of the inhibitory effect of the globus pallidus (GP) on the thalamic nuclei, and thus the inhibition of dopaminergic thalamocortical connections in the form of hyperkinetic syndrome [42]. That can be helpful in understanding the targets of DBS in TS: the internal globus pallidus (GPi) and central thalamic nuclei [7].

4.1. Targets and efficacy

The most commonly targeted areas for DBS in TS are the so-called thalamic centromedian-parafascicular complex (CM/Pf) and the ventral oral internal nucleus of the thalamus. In the globus pallidus two targets have also been distinguished: the posterior-ventral part (GPi-pov), responsible mostly for tic reduction, and the anterior-medial part, representing the limbic part of the GP and responsible for inhibition of tic-releasing urges. There are also limited reports on stimulation of the STN, GPe, NAc and ALIC. These last two targets were stimulated in patients with comorbid OCD or auto-aggressive behaviors. Analyses of treatment effectiveness show that GPi stimulation has a slight advantage over thalamic targets (almost a 55% reduction in *the Yale Global Tic Severity Scale* – (YGTSS) scores vs. 47% reduction, respectively). Most specific adverse events involving stimulation of the CM/Pf and thalamic nuclei are changes in the libido (both increases and decreases), while in the case of GPi stimulation, anxiety or depressive symptoms can be exacerbated. In 18% of TS patients, contamination of the stimulator area has been observed, caused by compulsive scratching of the surgical wound. The average risk of this adverse event in general DBS patient population is 3.7% [12, 42–44].

In the few randomized controlled studies investigating DBS targeting the thalamus for TS, the results were contradictory: in one study targeting the GP a significant decrease in tic severity was noted in very few patients (15%), while in another there was no significant difference at all [45–47]. These ambiguous results indicate that more controlled trials should be arranged, and that the choice of targets must be refined due to difficulties caused by the rich symptomatology of TS.

4.2. Indications, inclusion and exclusion criteria

The most commonly used inclusion criteria are as follows:

- Resistance to previous treatment (lack of or insufficient effect): at least three different psychotropic medications (mainly antipsychotics); at least one course of interpersonal therapy or CBT (at least 16 therapeutic sessions).
- A diagnosis of TS confirmed in accordance with DSM-5 criteria; a YGTSS score of at least 35 points; a GAF score under 50 points; disorder duration of at least five years.
- Age between 25 and 65 years.
- An IQ over 80.

Exclusion criteria include:

- Comorbidities: mental disorders (psychotic disorders, bipolar disorder, autism, severe personality disorders, psychoactive substance addiction, dementia), an unstable somatic state, disorders of the CNS (including epilepsy, PD, multiple sclerosis).
- Pregnancy [12, 48].

5. Anorexia nervosa (AN)

So far three different targets for DBS in anorexia nervosa have been proposed on the basis of clinical trials: the VS/Nac, BNST and subgenual cingulate cortex (SCC).

High frequency DBS of the VS and NAc has been performed in several case series studies, mostly in patients suffering from AN with comorbid OCD, depression or anxiety disorders. So far the results of these relatively small studies have been promising, showing improvement in both psychiatric symptoms and body mass index (BMI) [49–51]. No severe adverse events have been reported in these studies; in one case report by McLaughlin et al. [51] it was necessary to adjust the stimulation parameters due to the patient's mental state worsening. PET imaging of six AN patients showed a significant decrease of glucose hypermetabolism in the hippocampus, frontal cortex and lentiform nucleus [52]. We may speculate that the clinical improvement, based on mood and anxiety reduction in patients undergoing VS and NAc stimulation, contribute significantly to a reduction of AN severity and to weight gain.

In 2010, a case report on a depressive patient with comorbid AN was published. She underwent bilateral DBS implantation in the SCC. During the follow up, two relapses of depression were observed, but after the stimulation parameters were changed to unilateral right DBS of the SCC, her mental state became stable and her body weight significantly increased. With these parameters, AN remission lasted during the long-term follow-up despite a number of depressive exacerbations, mainly due to occasional stress [53]. In 2013, Lipsman et al. [54] reported a case series of six patients treated with DBS of the SCC. After nine months of observation, a stable improvement in psychiatric symptoms (mood, anxiety, obsessions and compulsions) was observed in four of these patients. Three patients presented significant BMI increase and maintained it during the follow-up period. One severe adverse event (a seizure during programming two weeks after surgery) was observed [54]. In a subsequent report on the one-year follow-up of 16 patients (with the previous six cases included), Lipsman et al. [55] observed significant improvements in BMI (>17.0) in eight cases, out of which six had achieved normal BMIs (>18.5). Significant improvements in mood and reductions in anxiety and obsessive-compulsive symptoms were observed. In both trials reported by Lipsman et al. [54, 55], significant changes in glucose metabolism were observed in PET imaging, mostly in the cortex, compared to baseline activity.

Summing up, the results presented so far are encouraging, especially in terms of VS/NAc and SCC stimulation for AN, but the reported studies are still underpowered to establish appropriate clinical recommendations.

6. Psychoactive substance addiction

Several case reports and case series studies have been published that suggest that DBS could offer potential benefit in substance addiction. Targeting the brain reward circuitry seems to be the most beneficial. Although long-term abstinence is not always achieved, reductions in substance use and cravings are often reported. In one case of bilateral NAc DBS in a heroin-dependent patient, abstinence was observed during a six-year follow-up period, which lasted even after DBS removal, which was necessary three years after the implantation surgery [56]. Another case of DBS in the same target in a heroin-dependent patient showed more than six months of abstinence [57]. In a recently published case series study, eight heroin addicted patients underwent ALIC/NAc DBS. Five of them maintained abstinence for more than three years; two relapsed after six months; and one was lost to follow-up three months after surgery. In the patients who remained abstinent, cravings for heroin were significantly lower during stimulation. No severe adverse events were reported. PET imaging of five of the patients (baseline and after six months of stimulation) showed significant differences in glucose metabolism in the cortex and corpus callosum [58].

In one case series study of NAc DBS in patients with alcohol addiction, two out of five patients achieved four years of abstinence, while the rest reported reduced alcohol consumption and cravings [59]. In another case series, all three patients reported dis-

appearance of cravings immediately after DBS was turned on, but only two of them maintained abstinence after one year of observation. The third remained abstinent for several months after surgery, then resumed alcohol consumption [60]. In some studies, cessation or significant reductions in nicotine intake and cravings were reported in patients with NAc DBS performed due to OCD, TS or alcohol addiction. A few patients maintained long-term nicotine abstinence [60–62]. Finally, one case of NAc and BNST DBS performed in a patient with severe cocaine addiction was reported. A significant decrease in cocaine intake was maintained after a 24-month follow-up period, with 68% of weeks free of consumption. Interestingly, no difference was observed during blinded turn-off periods, which was explained by the authors as either a placebo effect or longer-lasting changes in neuronal plasticity [63].

7. Alzheimer's disease

Data on the efficacy of DBS in Alzheimer's disease (AD) are still limited. Two main potential targets have been proposed so far: the nucleus basalis of Meynert (NBM) and the fornix.

In 2015, the results of a pilot study on NBM DBS including six mild to moderate AD patients were published. After one year of stimulation, a slower cognitive decline was observed, and four patients were considered responders [64]. Further studies brought additional evidence of the effects of NBM DBS on cognitive functions, showing that patients with less advanced AD are more likely to benefit from the treatment [65, 66]. All these studies reported good tolerance of treatment and no severe adverse events. In another published study involving 10 patients, the degree of atrophy of the fronto-parieto-temporal cortex observed in neuroimaging was proposed as a possible predictor of NBM DBS response [67].

In 2008, Hamani et al. reported a case of DBS performed to treat pathological obesity, targeting the fornix. Already after trial stimulation during the surgical procedure, the 50-year-old patient reported recurring memories and déjà vu experiences tracing back to memories from the time he was about 20. This effect persisted during post-operative DBS [68]. This case suggested that fornix stimulation could be beneficial for patients with impaired memory. In 2010, a phase I trial involving six patients with mild to moderate AD demonstrated the safety of fornix DBS. In five patients, cognitive decline (measured with *the Mini-Mental State Examination*) was reduced, and in four patients improvements in *Alzheimer's Disease Assessment Scale* cognitive subscale (ADAS-Cog) scores were observed after a six-month follow-up. Patients with less affected baseline cognitive performance showed better improvement after DBS [69]. Further observation revealed increases in glucose metabolism in two brain circuits: the frontal-temporal-parietal-striatal-thalamic and frontal-temporal-parietal-occipital-hippocampal one [70]. This observation suggests that neural plasticity is enhanced by DBS. Furthermore, after a one-year observation period, increases in hippocampal volume were confirmed by MRI [71]. Despite these encouraging results, a larger phase

II sham-controlled study proffered different observations. A trend toward clinical benefit was observed in a group of patients over 65, while younger patients showed tendencies toward further cognitive deterioration [72]. A further 12 months of observation of this cohort confirmed that the treatment offers possible benefits in patients over 65 [73]. An even larger trial involving 150 patients is currently being scheduled.

For now, both targets (the NBM and fornix) are promising in terms of cognitive improvements and safety, but larger controlled trials are needed to confirm the potential benefits from DBS therapy in AD patients.

8. Aggressive behaviors

Aggressive behaviors, particularly those called 'intermittent explosive disorder' (IED) in DSM-5, might occur in the course of many neurological and psychiatric disorders. So far many successful DBS treatments have been reported as single cases; different areas have been targeted. Bilateral DBS in the basolateral part of the amygdala was performed in a patient with mental retardation and autism, and a significant reduction of self-injuring behaviors was achieved [74]. Taira et al. [75] reported unexpected total disappearance of self-injuries in a patient who underwent bilateral GPi DBS due to dystonia in the course of Lesch-Nyhan syndrome. The authors suggested that the aggressive behaviors could have been a result of dystonia or were mediated by the basal ganglia.

Successful treatments have been also reported in cases of DBS targeting the posterior part of the hypothalamus (pHyp), mainly in the course of mental retardation. The largest cohort (seven patients) was reported by Franzini et al [76–78]. The enrolled patients presented IQs between 20 and 40; out of this group six responded with complete remission of aggressive behaviors or significant decrease in their intensity. Relapses were observed when DBS was off. In 2015, Harat et al. [79] reported a case of a patient performing dangerous aggressive behaviors in the course of cerebral palsy, mental retardation and OCD. First bilateral DBS of the pHyp was introduced, which resulted in significant improvement, but only for the first three weeks. Further adjustment of the stimulation parameters failed. A second pair of electrodes was implanted, targeting the NAc. With all four electrodes turned on, complete resolution of aggressive behaviors and a significant reduction in OCD and anxiety symptoms were observed, and the patient's social functioning and quality of life improved drastically.

9. Other mental disorders

Limited data are now available regarding the safety and efficacy of DBS in other psychiatric disorders, including bipolar disorder (BD), schizophrenia and post-traumatic stress disorder (PTSD). Based on the available reported cases of DBS performed in BD, Gippert et al. [80] came to the conclusion that patients benefited from treatment in a similar way to patients with MDD in terms of remission from depressive epi-

sodes. Manic or hypomanic episodes may emerge as a result of DBS (but they are also observed in MDD patients), but they respond well to adjustments of the stimulation parameters [80].

Recently, a case report of successful bilateral NAc stimulation in a patient with treatment-resistant schizophrenia was published as part of an early phase trial. After 11 months of treatment, stable improvement in both positive and negative symptoms was observed, followed by significant positive changes in functioning and quality of life [81].

A single case of treatment-resistant combat PTSD treated with bilateral DBS of the basolateral part of the amygdala was reported, also as part of a recently commenced early phase trial. After eight months of stimulation, a significant improvement in symptoms was observed, including nightmare frequency, sleep duration, anxiety, remission of dissociative episodes, and tolerance to stimuli reminiscent of the trauma [82].

10. Conclusions

The studies outlined here suggest that in a correctly selected target DBS may contribute to significant improvement in many different psychiatric disorders, especially in patients with OCD, which are very often refractory to other treatments. However, further studies are needed to determine the clinical applicability of this method. Currently, in Poland, there are institutions performing DBS in mental disorders – 10th Military Research Hospital in Bydgoszcz and Wroclaw Medical University together with the University Hospital in Wroclaw. A large multi-center trial on DBS in treatment-resistant MDD is being planned.

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