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Deep brain stimulation for the treatment of major depressive disorder: complex psychiatric aspects

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Dear Editor,

The fascinating review article on brain stimulation for treatment-resistant depression published by Michał Sobstyl and Angelika Stapińska-Syniec [1] raises many questions. In the following pages these questions are addressed, and commentary offered, on the application of deep brain stimulation (DBS) in major depressive disorder (MDD).

As the authors correctly stated, the issue is significant because, on average, 30% of individuals with MDD are classified as treatment resistant (TRD) [2, 3]. Usually, TRD is defined as two sufficient antidepressant trials that have failed to produce an "adequate response" [3, 4]. However, there is a lack of wide consensus as to this definition of TRD [5]. For instance, the biological process underlying the TRD is not entirely understood. All of these factors could result in disagreements over patient enrollment in DBS treatment [4]. Nevertheless, most of the relevant TRD algorithms rank DBS as the last-line treatment [3]. When both pharmacological and non-pharmacological approaches (including interventional ones, such as electroconvulsive therapy) augmented with psychotherapy have failed, DBS may be considered. The number of available treatment methods is constantly growing due to the introduction of new biological techniques; recently we have seen the emergence of esketamine and transcranial direct current stimulation [3, 4].

Furthermore, there are a variety reasons that could cause pseudo-resistance to treatment in MDD. Examples include factors related to the treatment itself (e.g. inadequate doses, too-short treatment times, the patient's non-adherence), comorbidity (e.g. personality disorders), misdiagnosis (e.g. depressive episode in bipolar disorder) or individual or social factors (e.g. entering the role of patient, unconscious need to be subject of care), to name just a few [5]. There are currently no definite clinical recommendations that would specify which patient subgroups would particularly benefit more from DBS treatment and perhaps should have been offered this approach sooner. However, because it is the most invasive treatment option for psychiatric disorders, the conditions of each patient should be carefully considered.

Some questions about DBS still remain open – placebo effect is one of them. Although it has been suggested that they are insignificant in individuals who are severely depressed, placebo rates are often very high in clinical trials for depression drugs' [6]. The next big question is what antidepressants (if any) the MDD DBS patient should be taking. There are not enough studies looking into antidepressant augmentation methods for DBS patients [6].

Based on the knowledge of other biological treatments for MDD, it is known that there is a risk of induction of a manic phase or a risk of an initial increase in suicidal intentions. Indeed, suicide attempts and manic episodes have already been described in patients undergoing DBS [2, 6], though a systematic review of the possible effects of deep brain stimulation on suicidality showed conflicting results [7]. There is still a lack of high-quality data on the long-term effectiveness of DBS in MDD [8]. Many biological treatments for MDD lose their effectiveness over time. This is partly due to the nature of the disorder itself. The more episodes of depression a patient has had in life, the greater the risk of another episode. When selecting a special group of „super-resistant" MDD patients with a long history of depressive symptoms, it is unclear whether such an effect could potentially occur in the long term (e.g. lifetime perspective) [9].

DBS in MDD is very promising and appears to be an effective method; however, there are still several concerns that require further research before it can be widely applied in everyday clinical practice.

Conflict of interest

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