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## Commentaries on "Subthalamic Deep Brain Stimulation in Obsessive-Compulsive Disorder: First German Experience and Future Outlook"

We read with great curiosity and interest the article by Wojtecki et al.[1] regarding a case of severe obsessive-compulsive disorder (OCD) treated with anterior subthalamic nucleus (STN) deep brain stimulation (DBS). Indeed, the authors reported on a patient with OCD patient; she was 41 years old and exhibited washing compulsions for 15 years that started with the birth of her daughter. Despite behavioral and medical therapy with a serotonin reuptake inhibitor (fluoxetine), her condition worsened over time with episodes of depression that were improved under clomipramine medication, without an effect on OCD. The baseline score of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score reached 38/40 and demonstrated a severe preoperative state. The Beck Depression Inventory was at 27, which underlined a depressive state as a comorbidity. In 2012, she underwent an operation consisting of the placement of 2 electrodes (3389, Activa PC System; Medtronic, Minneapolis, Minnesota, USA) within the "anteromedial region" of the STN. Surgery was uneventful, and stimulation was set bilaterally at 130 Hz, 60 μs, and 2.2 V. She developed dyskinesia on the left leg that resumed with the decrease of the stimulation. Her condition started to improve within 6 weeks of stimulation. Interestingly, depression scores improved first, followed at 3 months by clinically relevant improvement of the Y-BOCS score (27/40). Several adaptations of stimulation intensity were required at long-term follow-up. Finally, a bipolar stimulating mode was chosen on the 2 lowermost contacts. At 2-year follow-up, the patient reported a normal social and family life. She was working on a farm without washing compulsions. At 3 years, she had persisting major benefit without obsessions or compulsions (Y-BOCS score, 3/40).

This case report deserves some discussion as this therapy is not yet approved for OCD, and until now, the anterior capsule has been the only target approved in 2 European countries—the Netherlands and Belgium—for severe OCD. Only a few patients undergoing an operation on the STN for OCD have been reported in the literature. Furthermore, this case raises the question of a potential role of STN DBS in mood disorders.

The first comment is related to the powerful therapeutic effect obtained using the non-motor STN as a target to treat severe OCD. This is in line with several cases reports, including our already published one[2-4] and demonstrated by the only class 1 evidence paper published in the field of DBS and psychiatry.[5] It is interesting to note the low voltage used, which is in the range of what we typically observe and is much lower compared with the voltage required for stimulation of the anterior limb of the capsule.

The second comment is related to the dissociation of the effect of the stimulation on different symptoms over time. Wojtecki et al. reported here that the first clinical effect observed was not an improvement of the OCD symptoms that required several months of stimulation, but indeed an isolated antidepressive effect. The authors advocated a direct current spread to the median forebrain bundle, a structure that has been described to have a role in mood networks.[6] We also have observed such dissociation in one of our patients with STN DBS for OCD with improvement in depression preceding improvement in OCD for several weeks. Typically, however, mood is improved once patients can feel a strong therapeutic effect on the OCD symptoms, so that it is not possible to state whether mood improvement can be directly related to stimulation itself or have to be interpreted as secondary mood improvement in response to the strong effects of STN DBS on OCD. However, the effect of STN DBS on mood in parkinsonian patients has already been reported.[7] We also commonly observed, during the period settings of stimulation parameters, a transient increase in anxiety along with psychomotor agitation and impulsivity induced by stimulation of the non-motor STN in a voltage-dependent manner before improvement in OCD symptoms. This side effect systematically resolves when decreasing the intensity of the current used. A slower increase over longer periods eventually can allow to improve OCD symptoms avoiding such side effects, but the therapeutic window can be small.

Wojtecki et al. discussed the relationship between the antidepressive effect observed and a possible current diffusion to the median forebrain bundle. Schlaepfer and Coenen[6] have shown improvement of major depression with stimulation targeting the medial forebrain bundle. Given the close proximity of the limbic medial tip of the STN and the medial forebrain bundle, it is difficult to know whether the reported antidepressive effects in the present report is related to stimulation of the fiber tracts or the limbic STN territory. Indeed, one must also acknowledge that the anterior STN is directly connected to the limbic and associative cortex, and that the stimulation of the hyperdirect non-motor cortico-STN tract might also be responsible for mood changes. This has already been mentioned in parkinsonian patients undergoing operation in the motor STN.[7] Indeed, looking at the anatomy, the site of stimulation used to target the medial forebrain bundle encompasses limbic "tributaries" arriving in the STN trough the medial forebrain bundle that have been illustrated by fiber tracking.[8] This might, at least in part, explain the mood changes. If this hypothesis is right, it is likely that stimulation of the anterior STN can also affect those fibers and, consequently, can interfere with mood via the limbic circuitry. Finally, stimulation of limbic and associative territories of the STN can also affect mood by influencing the direct and indirect limbic and associative striatopallidal basal ganglia pathways.

Our third comment is related to the appearance of dyskinesia of the left leg induced during the ramping up of the voltage, in the context of normal dopamine condition. We already have noticed this unexpected side effect in some of our patients, and it seems related directly to the effect of the high-frequency stimulation applied within the posterolateral sensorimotor territory of the STN, in the absence of any dopamine deficit. (We have also observed this in patients with severe epilepsy and implanted in the motor STN, for example.) This also may reveal that the stimulated contacts were close to the motor region of the STN, which seems to be the case when looking at the postoperative magnetic resonance image in which the contacts seem to be more posterior in the STN, in a plane located at the level of the anterior border of the red nucleus. Anyway, the powerful therapeutic effect obtained

here demonstrates that the contact used could eventually module the non-motor circuitry as already advocated.

Finally, this case report from a different European group illustrates once again the potential role of STN in mood and psychiatric disorders. We do believe that data accumulated in the literature reinforce the importance of the non-motor STN as an alternative target to treat OCD patients.

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