Editorial commentary

Deep brain stimulation in Tourette syndrome: the known and the unknown

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How much data are needed to conclude the effectiveness of deep brain stimulation in Tourette syndrome?

The paper by Johnson et al[1] is based on a collaboration with the International Tourette Syndrome (TS) Deep Brain Stimulation (DBS) database and registry. This TS DBS database/registry has been initiated in 2012 by a group of researchers and clinicians led by Michael Okun. They aimed to collect as many data as possible to increase the database on efficacy, safety and surgical approaches of DBS in TS. Without any doubt, there is a critical need to increase current knowledge since the absolute number of patients who received DBS is still low and until today only a very limited number of randomised controlled trials (RCTs) including only a small number of patients have been performed. Twenty years after the introduction of DBS in the treatment of TS, less than 200 patients have been reported in the literature and data of only five RCTs have been published including 3 to 16 patients (altogether N=43 patients). Furthermore and in contrast to most other indications, in TS the optimal target is still unknown. So far, 10 different brain areas have been suggested including four targets in the centromedial (CM) thalamus, the anteromedial and the posteroventrolateral part of the globus pallidus internus (GPi), the globus pallidus externus, the nucleus accumbens, the anterior limb of internal capsule and the subthalamic nucleus.

This is the first study that aimed to identify the optimal target for DBS in patients with TS including a large sample (N=110 patients from 13 different institutions across three different continents) by using the DBS TS database/registry. In line with recent results based on this database/registry[2] and a meta-analysis,[3] the authors found a significant improvement of tics and obsessive-compulsive behaviour after DBS (p<0.01). Remarkably, best improvement in tics (40%) was reached only 13 months after surgery.

However, the authors failed to identify any significant differences across different targets. The most often used targets (GPi and CM thalamus) were effective in some patients, but ineffective for others.

This important work sheds further light on the value of DBS in TS, but in parallel raises several important questions. While the utilisation of the TS DBS database/registry is a major advantage, at the same time it is the most significant limitation of this study: the registry aims to combine outcome information from a variety of centres worldwide without restrictions on investigators or groups who wish to join the project. In addition, there is no limitation to the maximum data necessary to register a case. Although researchers were encouraged to submit positive as well as negative results, it can be assumed that there is a relevant reporting bias towards more positive experiences. Finally, the majority of data are based on case reports and open uncontrolled studies, but not on RCTs. This is of utmost importance since the largest RCT[4] failed to demonstrate a significant improvement of tics at the end of the 3-month double-blind period, but tics were decreased after the following 6-month open-label period. In line with the data reported in this issue by Johnson et al,[1] the authors[4] argued that in TS the time to respond to DBS is on the order of multiple months and optimal parameter settings are needed. However, alternatively one may speculate that open uncontrolled data are influenced by several other factors including spontaneous fluctuations, environmental and psychosocial factors, but also the presence of functional 'tic-like' movements as suggested recently.[5]

Similarly, the fact that the authors failed to identify differences between different targets can be interpreted in two different ways: it can be speculated that in TS it is important to modulate an abnormal cortico-striato-thalamo-cortical network instead of stimulating a single circumscriptive brain area to restore abnormal function; but alternatively, it can also be argued that TS DBS is not superior to sham stimulation—as suggested by some of the small RCTs—and therefore stimulation of several different brain areas results in comparable clinical effects.

Although the authors were able to use a unique sample for their analyses and results based on such databases are urgently needed, when interpreting the results it must be taken into consideration that these results can only be as good as the underlying database. Unfortunately, in TS, the database is still very weak and therefore final conclusions on the efficacy of DBS cannot be drawn. Remarkably, even several years after the introduction of DBS in the treatment of TS, even severely affected patients are still very cautious to decide for DBS.

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