Use of Nexstim Navigated Brain Therapy (NBT®) System in Treatment of Major Depressive Disorder – initial experience

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Background

During last decades, the use of excitatory high-frequency rTMS (10Hz or 50Hz thetaburst), targeted to the dorsolateral prefrontal cortex (DLPFC) of the left hemisphere, has been established as a safe and effective treatment for adult patients suffering from Major Depressive Disorder (MDD) who have failed at least one pharmaceutical drug in their current episode. Several TMS devices have obtained FDA clearance for this indication and entered the market.

In the therapy approach used, most marketed devices target rTMS to the approximate location of the DLPFC. Targeting is done by localization of the motor cortical site of the Abductor Pollicis Brevis (APB) hand muscle, and then measuring e.g. 5 cm anteriorly along the scalp surface ('5 cm method'). However, it has been demonstrated that this results in suboptimal targeting of the intended DLPFC. In a study comparing the 5 cm method to localization performed using the patient's own MRI and a neuronavigation device, it was determined that the 5cm rule properly localized stimulation to target in only 7 of 22 subjects (31%) (Herwig 2006).

The first neuronavigated TMS device allowing patient-specific targeting of DLPFC, the Nexstim NBT® system, obtained FDA clearance for treatment of MDD and was launched on the US market in May 2018 (Figure 1). The NBT2 system utilizes the same SmartFocus® technology as Nexstim's diagnostic Navigated Brain Stimulation (NBS) device, previously FDA cleared for pre-procedural localization of the motor cortex to its correct gyrus and used by neurosurgeons for functional brain mapping prior to neurosurgery, most commonly in patients with brain tumors.

In the SmartFocus® technology, the patient's MRI dataset is used to link the location of the TMS-generated stimulating electric field to the individual patient's cortical anatomy. In clinical studies in brain tumor surgery, the NBS system localized the motor cortex in all patients to the same gyrus as intraoperative direct cortical stimulation (DCS). According to the operating neurosurgeons, the results of preoperative mapping of the motor cortex with NBS are as accurate as DCS (Forster, 2011, Picht 2011, for clinical meta-analysis, see Raffa 2019).

In a comparison between classic 5cm and NBS/NBT targeting of DLPFC, it has been determined that the median distance between the therapy target obtained using the 5cm method is 2cm posterior from the location (between the anterior and middle thirds of the middle frontal gyrus and between the superior and inferior frontal sulci) as determined by NBS/NBT technology (Ahdab, 2010).

As NBT allows accurate targeting of the patient-specific DLPFC and not the average DLPFC, the use of the system in clinical practice might yield better clinical outcomes. However, at present there is no clinical literature on the use of NBT in the treatment of MDD.

As we at Island Psychiatry P.C., a multidisciplinary mental health practice serving three locations in Long Island, New York, were the first in the U.S.A. to introduce an NBT system into a routine clinical process, we decided to review and report the results seen in the first 10 patients completing treatment.

Figure 1: NBT system incorporating TMS stimulator, stimulating coil, EMG and navigation software in a single clinical system. The system treatment chair, head rest and coil holder allow patient comfort and maintenance of the correct head position relative to the stimulation coil during rTMS.

Patients and methods

Experiences in the first 10 consecutive patients (6 female, 4 male) completing treatment of MDD with the Nexstim NBT system at Island Psychiatry P.C., are reported. At start of therapy, the patients' mean age was 42 years (range 18-71), their mean score on Beck's Depression Inventory (BDI) 31.4 (sd 13.2) and mean score on PHQ-9 Health Questionnaire 14.8 (sd 6.5).

A stereotactic 3D T1 MRI dataset with 1.5x1.5x1.5mm voxels was obtained. After loading the MRI dataset to the NBT System, and placement of EMG surface electrodes over the Abductor Pollicis Brevis (APB) muscle, mapping of motor cortex was performed to localize the cortical representation area of APB and its motor threshold (MT) determined with the assistance of the NBT software.

Next, the DLPFC and other possible treatment targets were marked on the 3D head in the NBT software. For DLPFC, the optimal anatomic target was identified using a previously published method of clinical target validation (Mylius et al, 2013). The NBT treatment coil was then moved and fixed to a location which ensured that the maximum electric field induced by TMS was delivered to the intended target (Figure 2).

On average patients were treated over 37 treatment sessions. In all patients therapy was initiated with an rTMS protocol targeting left DLPFC (10Hz, 3000 pulses, 120%MT) delivered over 19 minutes. After 4-7 sessions, the protocol was modified include rTMS delivery to the right DLPFC (1Hz, 550 pulses, 120%MT) in 7 patients. In three patients the protocol was modified so that 1600 pulses were delivered to the left DLPFC at 10Hz, 550 pulses to the right DLPFC at 1Hz and additionally 250 pulses to both left and right supplementary motor areas (SMA) at 1Hz at 110% MT.
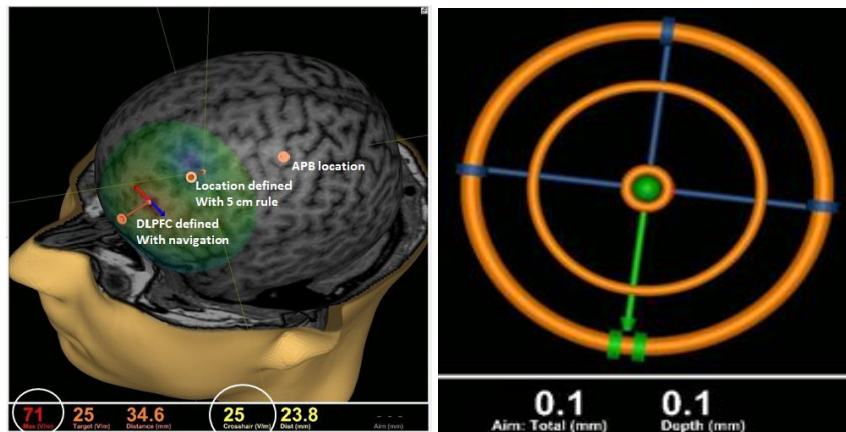
Figure 2

Figure 2: Left) NBT system software showing the patients anatomic left DLPFC stimulation target as per Mylius et al., 2013, the target which would be stimulated if targeting was based on the classic 5cm targeting method, and the APB location determined with the NBT system and used for MT determination.

Right) The targeting tool of the NBT software. The SW monitors the coil position, tilting and orientation of the induced electric field relative to the target. Should accuracy be compromised, the colour would change from green to yellow and red with increasing loss of accuracy allowing the operator to reposition the coil.

Results

The treatment was well tolerated by the patients. There were no serious adverse events. One patient (the first treated) experienced transient ocular migraine after two of the treatment sessions. The patient completed all of his 36 treatment sessions. In 2 patients, stimulation intensity was decreased from 120%MT to 115% and 95%, respectively, to improve patient comfort during stimulation.

Treatment outcomes were good. Five of the 10 patients (50%) were in remission at end of treatment while 7 of the 10 (70% had obtained a clinical response of at least 50% decrease in BDI/PHQ9. The mean BDI score at end of treatment was 15.9 and mean PHQ9 score 8.0 (Figure 3). The average decrease on BDI from start to end of treatment was 49.6% and the decrease in PHQ9 46.0%. Decreases in both were statistically significant ($p<0.01$ and $p<0.02$, for BDI and PHQ9, respectively).

Figure 3. BDI and PHQ9 scores (mean +SD) before and after treatment
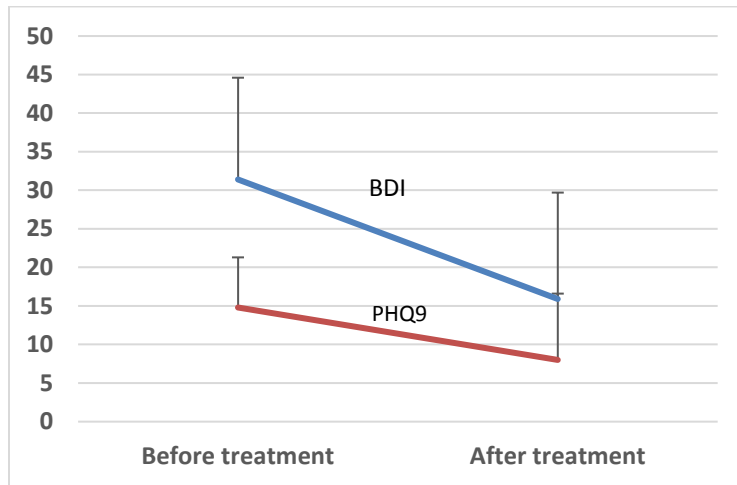
Discussion and Conclusion

The initial clinical results reported provide further confirmation of the well-established safety and efficacy of rTMS in the treatment of adult patients with Major Depressive Disorder.

Based on our experience, Nexstim NBT can be easily integrated into the routine workflow of these patients. During treatment planning, the software facilitates rapid localization of the APB, MT determination and targeting of rTMS. During therapy it makes possible accurate and reproducible stimulation of the intended anatomic targets over several treatment sessions.

Clinically, the patient-reported outcomes obtained in the first 10 completed patients (50% remission, 70% clinical response rate) were higher than what was reported for naturalistic open label clinical use in a well-conducted series (remission 26.5-28.7%, response 41.5-56.4% for patient reported measures, Carpenter,2012). Future clinical work will demonstrate whether these higher remission and response rates are reproduced in larger patient series.

References

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