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Electrical field measurements and simulations of the H7 and D-B80 coils: Non-equivalence of the TMS coils for obsessive compulsive disorder

Dear Editor,

In 2018, the FDA cleared deep transcranial magnetic stimulation (dTMS) with the H7 coil for obsessive-compulsive disorder (OCD) treatment following a successful pilot randomized-controlled trial (RCT) [1] and a subsequent double-blinded placebo-controlled (DBPC) multicenter trial [2]. Two years later, TMS with the D-B80 coil was also FDA-cleared for the same indication on the basis of claimed substantial equivalence. While both coils appear to be bent figure- 8 coils, they differ in diameter of their circular wings and distance between the two wings. In addition, the D-B80 has a rigid fixed angle between the circular wings while the H7 is a flexible coil that conforms to the shape of the head.

We compared the induced electric field (EF) characteristics between the coils in the treatment position for OCD through EF measurements of a saline solution head model and high-resolution electric field simulations of various anatomical models. Three-dimensional EF distributions of the H7 and D-B80 coils were measured in a phantom head-model filled with physiologic saline solution, at the treatment location over the medial prefrontal cortex (mPFC). The intensities were adjusted to the average percentage of the maximal stimulator output (MSO) required to achieve resting threshold stimulation of the foot. This was 53% of MSO for the D-B80 coil (connected to a MagPro R30 stimulator, maximal output 1.9 kV (MagVenture, Denmark)), based on previous studies [3,4], and 54% for the H7 coil (connected to a BrainsWay stimulator, maximal output 1.7 kV (BrainsWay, Israel)) [1–2, BrainsWay data on file]. At these power outputs, the peak coil currents were calculated to be 3.64 kA for the D-B80 and 3.18 kA for the H7.

To complement the phantom measurements, E-field simulation was carried out using the Sim4Life (S4L) platform (ZMT Zurich MedTech. Sim4Life 6.0) for electromagnetic simulations (simulation performed at 3.5KHz). The D-B80 coil model [5] had two layers including three windings on top and four windings beneath with outer and inner diameter of 95 mm and 67 mm, respectively. The H7 coil model (CAD file provided by the manufacturer), had two layers of four elliptically shaped windings each, one on top of the other, whose major axis ranged from 130 to 70 mm and minor axis from 105 to 55mm (Fig. 1a). The simulation was carried out over a variety of models and parameter spaces (22 models): Three high resolution anatomical models of the Virtual Population (ViP) family (Duke, Ella, Thelonious), including their homogeneous versions, and eight members of the Population Head Model (PHM) repository, with two sets of conductivity values: The first set (PHM v.1) corresponds to the low frequency tissue database of IT'IS Foundation, while the second (PHM v.2) includes typical conductivity values for TMS simulations.

The distribution of values of EF intensity was determined in the following areas relevant to the circuitry of OCD: (i) pre-supplementary motor area (pre-SMA), (ii) inferior frontal gyrus (IFG), (iii) dorsolateral prefrontal cortex (dlPFC), (iv) orbitofrontal cortex (OFC), (v) dorsal anterior cingulate cortex (dACC). These regions are considered part of the cortico-striato-thalamic-cortical (CSTC) circuitry and have been implicated in the pathophysiology of OCD [9]. Maximum EF value (E_{max}), percentage of cortical volume (V_{100}) and maximal depth (d_{100}) for which EF $\geq$ 100 V/m [6–8] were compared using paired *t*-test.

Both phantom measurements and simulation showed that the H7 coil stimulates much larger and deeper brain volume and induces higher field intensities than the D-B80. Indeed, for the D-B80 at the treatment location (PFC), the field is considerably weaker, and supra-threshold field is induced only in very shallow brain layers. In all models and in the phantom measurements, the V_{100} was significantly larger for the H7 over the D-B80. The mean $\pm$ SD of V_{100} were 11.1 $\pm$ 5.9 cm^3 for the D-B80 and 40.3 $\pm$ 24.3 cm^3 for the H7. In terms of percentage of the whole brain, the stimulated volume mean $\pm$ SD were 0.91% $\pm$ 0.48% cm^3 for the D-B80 and 3.36% $\pm$ 2.04% cm^3 for the H7 coil. This difference is highly significant ($p < 0.0001$, $t = 7.04$, effect size 1.2). In addition, the H7 induces significantly higher E_{max} in the brain (mean $\pm$ SD: H7: 139 $\pm$ 16; D-B80: 114 $\pm$ 12 V/m, $p < 0.0001$, $t = 11.08$, effect size 1.8) and higher d_{100} (mean $\pm$ SD: H7: 31 $\pm$ 13; D-B80: 19 $\pm$ 11 mm, $p < 0.0001$, $t = 6.17$, effect size 1.03) in all models.

Fig. 1b presents the percentage of brain volume stimulated by each coil for all the 22 models and for the phantom field measurements. In all models the H7 stimulates two to five times larger brain volume. A bubble plot is shown in Fig. 1c where the y axis is the d_{100}, and for each model is presented a bubble for the D-B80 (blue) and H7 (red) coils, with the bubble size proportional to V_{100} value which is also shown in each bubble.

The distribution of values of EF intensity within the five brain regions (dACC, dlPFC, IFG, OFC and pre-SMA) were computed for all the 22 head models. Comparison of the EF distribution using Wilcoxon matched-pairs test (after failed normality test) found a highly significant difference between the coils ($p < 0.0001$) in all five brain regions.

There is high variability in the results between the various models, most probably due to the large differences in size and

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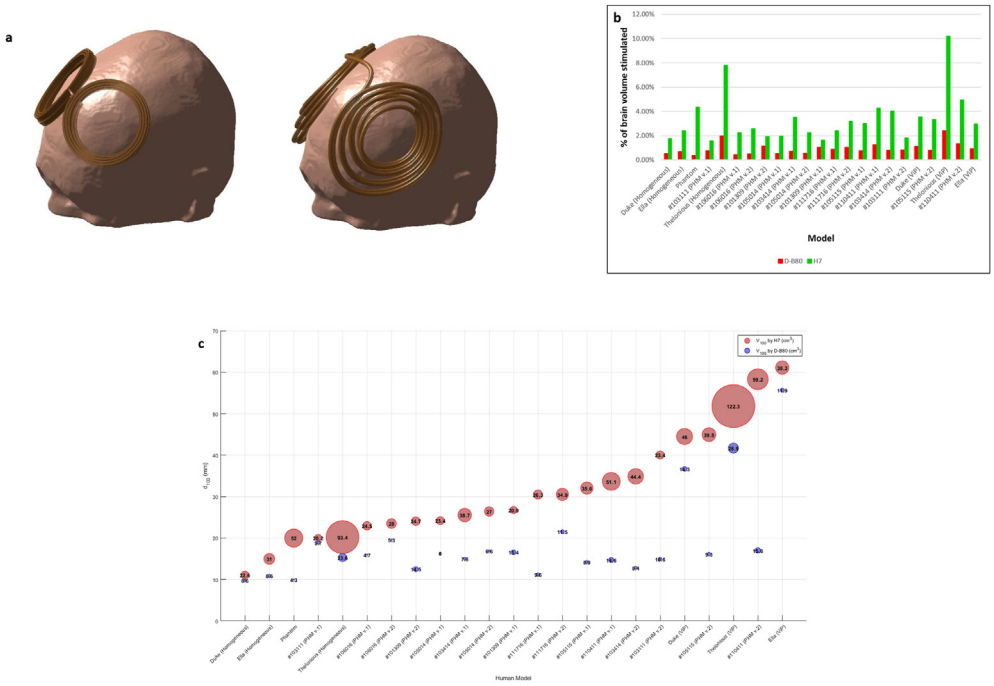

Fig. 1. a. Sketches of the D-B80 (left) and the H7 (right) coils windings at the treatment position over the medial prefrontal cortex of a human head. b. Percentage of the brain which is stimulated at or above 100 V/m (V_{100}) by the D-B80 (red) and by the H7 (green), shown for each of the 22 simulated head models and for the phantom field measurements. c. A bubble plot showing for each model the d_{100} (y axis) and V_{100} (bubble size and value inside bubble) for the D-B80 (blue) and H7 (red) coils. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

internal compartmentation. Yet, all the methods and models found that the H7 stimulates significantly broader and deeper brain volume compared to the D-B80. The aggregate of results clearly indicates that many prefrontal structures are stimulated by the H7 but not by the D-B80. Among those are structures within the pre-SMA, IFG, dlPFC, OFC and the dACC, all of which comprise parts of the CSTC circuitry and have been implicated in the pathophysiology of OCD [9].

Double-blinded RCTs [1,2] have demonstrated that dTMS with the H7 over the mPFC-dACC is a safe and effective intervention for the alleviation of OCD symptoms in patients who failed to receive sufficient benefit from previous treatments. The response rate compared to sham treatment was significantly higher for up to one month. Recently it has been demonstrated that in real-world clinical practice, dTMS with H7 over mPFC-dACC was beneficial for the majority of OCD patients (98/135, 73%) with the onset of sustained improvement usually occurring after 20 sessions [10].

Regarding clinical experience with D-B80 in OCD, one open-label study in 20 OCD patients found that 50% responded to treatment [11], while no RCTs have been reported to date. Due to the substantial differences found between the coils, the clinical efficacy in alleviation of OCD symptoms demonstrated with the H7 cannot be directly assumed for the D-B80, since the TMS underlying biophysical mechanism is known to be associated with the induced EF. The clinical efficacy of the D-B80 in OCD should be adequately demonstrated in the context of large RCTs and independently of the H7, from which it is substantially different in terms of induced EF distribution in the brain.

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Declaration of competing interest

Dr. Roth and Dr. Zangen are key inventors of deep TMS technology and have financial interest in BrainsWay. Dr. Harmelech, Dr. Zibman and Dr. Pell are BrainsWay employees. Dr. Tendler has a financial interest in BrainsWay and a clinical and research TMS center. Ms. Tzirini, Dr. Samaras and Dr. Kimiskidis have no relevant financial interests.

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