

## 1 **Supplemental Material**

### 2 **Methods Continued**

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#### 4 *Surgical Targeting*

5 DBS and MRgFUS share similar targeting coordinates. MRgFUS lesioning is targeted 14-15mm  
6 lateral from the midline (or 11mm lateral from the third ventricle wall), anterior from the  
7 posterior commissure (PC) by 1/3 to 1/4 the inter-distance between the anterior commissure  
8 (AC) and the PC, and 2mm superior to the AC-PC line.<sup>1</sup> DBS targeting is the same apart from  
9 being slightly inferior, at the level of the AC-PC line.<sup>2</sup> Furthermore, microelectrode recordings  
10 are used to refine the targeting intraoperatively by identifying the VIM-VC border. The  
11 implanted lead is then placed 2mm anterior to the recording tract.

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#### 13 *Image Acquisition*

14 The image acquisition parameters have been previously described by our group.<sup>3</sup> In brief, high  
15 spatial resolution pre- and postoperative structural imaging were collected. Preoperative  
16 (immediately prior to procedure) and postoperative (1 or 2 days post-procedure) imaging  
17 consisted of 1.5 or 3-Tesla T1 3-dimensional spoiled gradient echo (3D-SPGR, General Electric  
18 [Boston, MA] Signa Excite/HDxt scanner).

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#### 20 *Lead Localization and Lesion Segmentation*

21 The method used for lead localization has been previously described by our group.<sup>3</sup> It was  
22 performed based on the acquired high spatial resolution structural imaging and utilized Lead-  
23 DBS v2.0 software (<https://www.lead-dbs.org/>).<sup>4</sup> Pre- and postoperative images were linearly  
24 registered using SPM12 (<https://www.fil-ion-ucl-ac-uk/spm/software/spm12/>)<sup>5</sup> and nonlinearly  
25 normalized to a Montreal Neurological Institute (MNI) template brain (ICBM 2009b NLIN  
26 asymmetric) using ANTs SyN and subcortical refinement.<sup>6</sup> To localize DBS electrodes the  
27 semiautomated trajectory reconstruction function in Lead-DBS was used and manually refined as  
28 necessary. Activation volumes (VTAs) were estimated using the DBS stimulation settings at  
29 follow-up as per previously published methods.<sup>7,8</sup> DBS stimulation parameters used from  
30 activation volume modelling were as follows (mean  $\pm$  standard deviation): voltage (V)  $2.5 \pm 0.6$ ,  
31 frequency (Hz)  $100.2 \pm 52.7$ , pulse width ( $\mu$ s)  $116.7 \pm 53.0$ . Contact configuration was  
32 monopolar 60.6%, double monopolar 3.0%, bipolar 33.3%, interleaved 3.0%.

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34 The MRgFUS lesion segmentation and image processing methods were performed as previously  
35 described.<sup>9</sup> Briefly, immediate post-operative T1-weighted MRI images were used for manual  
36 segmentation. These were rigidly aligned (6df) to the preoperative T1-weighted image using FSL  
37 (FMRIB, Oxford, UK, <http://www.fmrib.ox.ac.uk/fsl/>) and the MincTools software kit (BIC-  
38 MNI, Montreal, Canada, <https://bic-mni.github.io/>) used to manually delineate the lesion in axial  
39 planes as described by Wintermark et al.<sup>10</sup> Using the Advanced normalization tools (ANTs,  
40 <http://stnava.github.io/ANTs/>) the preoperative MRIs were linearly and nonlinearly transformed  
41 to MNI space.<sup>11</sup> The derived transforms were then applied to the lesion mask.

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#### 43 *Statistical analysis*

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## 45 Probabilistic Voxel-wise efficacy maps

46 Probabilistic voxel-wise efficacy maps providing insight into spatial patterns of response to  
47 treatment were generated as previously described.<sup>12</sup> Briefly, each transformed VTA or lesion was  
48 weighted by clinical improvement (percent improvement from baseline) and voxel-wise mean  
49 improvement computed by averaging the weighted values. Using unweighted frequency maps (n-  
50 map), denoting the number of VTAs or lesions overlapping at a given voxel, the raw average  
51 maps were thresholded at 10% to exclude outlier voxels. The final average maps were masked by  
52 the n-maps and then thresholded using a Wilcoxon signed-rank test ( $P < 0.05$ , at each voxel). In a  
53 similar fashion, to identify voxels that, within each group, were associated with above/below  
54 average outcomes, the clinical improvement scores were z transformed for both groups of  
55 patients, and average voxel efficacy maps were calculated as described above.

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## 57 Structural connectivity analysis

58 Structural connectivity analysis was performed as previously described.<sup>3,12</sup> Briefly, this analysis  
59 makes use of a 12 million-streamline, whole-brain tractogram created from multishell diffusion-  
60 weighted MRI (dMRI) data<sup>13</sup> of 985 subjects created utilizing generalized q-sampling imaging  
61 and Lead-Connectome.<sup>14</sup> In the first step, all streamlines touched by each lesion or VTA were  
62 identified. Next, unweighted frequency maps were generated to identify shared streamlines  
63 implicated in each treatment across the entire group of patients, denoting the number of VTAs or  
64 lesions touching a given streamline. Group tractograms of shared streamlines were thresholded at  
65 75%.

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