

Appendix 1 to Blumberger DM, Maller JJ, Thomson L, et al. Unilateral and bilateral MRI-targeted repetitive transcranial magnetic stimulation for treatment-resistant depression: a randomized controlled study. *J Psychiatry Neurosci* 2016. DOI: 10.1503/jpn. 150265

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Details of DLPFC Localization and Scalp to Cortex Calculation

This procedure required the use of two computer programs for analysis of each participant's scans in order to obtain data on the scalp to cortex distance (SCD). MRICro software was used in the initial analysis of each acquired scan, allowing for localization of motor cortex and DLPFC for SCD measurements (Rorden and Brett, 2000). The specific area of motor cortex that controls the adductor pollicis brevis (APB) muscle was located by the researcher on the raw scans using the guideline that it was on the lateral edge of the "inverted omega" or hand knob of the motor cortex. SCD at both motor cortex and DLPFC were calculated using 'virtual calipers' (within the Line Profile module of Analyze), with each measurement taken tangential to the skull to replicate the position of the TMS coil.

In order to localize the DLPFC stimulation site, a structural MRI (high resolution, T1-weighted, 128 slices TR=9.08ms, TE=2.70, matrix size=256x256, slice thickness = 1.40mm, 1.5T Signa General Electric, Milwaukee, US) was co-registered to participants' heads using a magnetic tracking device (miniBIRD, Ascension Technology Group, Shelburne, Vermont, USA) for coil-to-cortex co-registration. The neuronavigational protocol was conducted using the raw scan yoked to the normalized images by following a number of steps. First, the participant's head was placed in a frame that kept the head still. Each fiducial location on the MRI scan was registered to the matching point on the

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person's head, by registering the location of those fiducials in 3D Talairach space with the miniBIRD magnetic wand position on the head, using MRIreg. MRIreg computes a multiple linear regression to map the marker coordinates onto MRI coordinates (least squares linear estimation). Second, as a quality control, the reliability of the localization technique was confirmed by navigating the sensor/wand to known anatomic points such as nose or ears on the nonskull stripped scan and confirming that these points were accurately identified on the MRI scan. Third, the MRIreg "tracker" mode was used. This technique has been reported to be more effective in localizing the DLPFC than the standard '5-cm method' (Herbsman *et al*, 2009; Peleman *et al*, 2010; Rusjan *et al*, 2010). For optimal stimulation of the DLPFC an area between the centre of BA 9 and the border of BA 9 and 46 was targeted, based on the conservative definition of these areas in previous research (Rajkowska and Goldman-Rakic, 1995). Stimulation was targeted at the Talairach coordinates of $x = -45$ or 45 (depending on hemisphere), $y = 45$ and $z = 35$. This localized stimulation is approximately over the junction of the middle and anterior thirds of the middle frontal gyrus and is very close to the junction of BA 9 and 46. DDLPFC and DM1 were measured in Analyze 12.0 (Mayo, USA) using the Line Measure module.

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