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Anatomically based targeting of prefrontal cortex for rTMS

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Keywords

rTMS; neuronavigation

INTRODUCTION

Repetitive transcranial magnetic stimulation (rTMS) is an efficacious treatment for major depressive episodes(1). Most clinical applications of this technology are based on probabilistic targeting methods which do not account for individual anatomic variability (e.g. the so called “5-cm rule”) or factor primarily the skull and not brain size differences (e.g. using the International 10–20 EEG system(2)(3). This may lead to suboptimal clinical responses when compared to individualized targeting techniques based on structural brain scanning(4–6). Research studies investigating the mechanism of action of TMS and those utilizing it as a tool usually require the type of precision not offered by probabilistic targeting methods.

Accurate targeting with TMS typically acquire a high resolution T1 scan of the head and a virtual stereotaxic system to achieve real time localization to the nearest scalp point to their target of interest (e.g. (4,7)). Such systems require dedicated computing hardware, software and optical sensing equipment. They are expensive and may be complicated to use.

Andoh et al.(8) devised a method of targeting rTMS using a structural anatomical scan only and simple image preprocessing step. The triangulation-based MRI-guided method identified a cortical target derived from individual MR data. Using three wires to determine the corresponding scalp target, they showed good accuracy and reproducibility in localizing the cortical M1 area. We used the same technique to target a fixed prefrontal coordinate. In this report, we discuss the real world accuracy of this relatively simple and inexpensive anatomically specific targeting procedure. We also propose a modest simplification of the original technique: in practice, full triangulation is not necessary.

METHODS

Fifteen psychiatrically and medically healthy controls (mean age of 29.5 +/− 8.1 years) were recruited. Each underwent high resolution T1 scans (isotropic voxels, 1×1×1mm;

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176×256×256 voxels, Siemens 3T scanner, Siemans Medical Solutions USA, Malvern, Pennsylvania). Participants provided informed consent for this protocol as part of an IRB approved trial of rTMS effects on functional connectivity. A standard location in left midfrontal gyrus (MNI-152: −45.5, 44.5, 40.4) was transformed to each individual's coordinate space using a 12 degree of freedom affine transformation using the FSL FLIRT utility(9). We used the methodology specified in Andoh et al.(8) to triangulate a location on the scalp which corresponded to the target per each individual. Briefly, using the BrainVisa software we found the nearest neighbor scalp location to the subject space transformed standard coordinate. Software automatically supplied distances from this coordinate to the nasion, left and right tragus. We then measured these distances using electrical wire and marked the intersection of all three on a Lycra swimming cap. We placed a fiducial with long axis in anterior posterior direction on this location taped to the Lycra swimming cap fitted to the subject's head before acquiring another T1 scan. This last T1 scan was used in order to record fiducial location in order to make the confirmatory measurements below—it is not however necessary.

Using the second scan one operator (TH) chose the nearest cortical point to the center of mass (CoM) of the fiducial using a modification of the fiducial scalp to cortex measurement method described elsewhere(10). We chose the coronal slice 6mm posterior to the CoM and selected the gray matter cortical voxel nearest the CoM. All distances are Euclidean, i.e. $\sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$. We report all coordinates in MNI-152 space.

RESULTS

The nearest cortical point to the CoM of each fiducial was an average of 9.4mm (N=15; maximum = 13.5mm, minimum = 7mm, standard deviation 2.1mm, median 9.2mm) distant from the fixed cortical target (Figure 1). The average of the actual targeted standard coordinates was (−42.0, 42.9, 35), a distance of 6.4 mm from the targeted location in which most of the inaccuracy is accounted for by inferior-superior axis inaccuracy.

DISCUSSION

We report on the results of using a novel triangulation technique for targeting a fixed prefrontal coordinate. This method offers a relatively simple way of targeting a fixed coordinate that utilizes a structural scan but no other dedicated hardware. It produces targeting which, on average, is less than a centimeter away from the specified prefrontal target. Given that that use of stereotaxic techniques is itself associated with targeting error on the order of 3 mm(8), a small distance relative to the 1–2 cm area of rTMS stimulation, this method is a viable alternative to more complicated and costly stereotaxic targeting paradigms. In addition, it can be used to any target on the cortical surface. However, unlike probabilistic targeting techniques, this technique still requires a structural MRI scan.

Differentiation of cortical tissue function likely happens on a 3–6 mm resolution(11) which may yield both a clinical and research advantage to using MRI based methods. And unlike probabilistic methods, the triangulation and stereotaxic methods allow arbitrary targeting of any cortical coordinate. And although, the 10–20 EEG targeting method(2) and variants(3) may target Brodmann areas 9 and 46 more consistently than the 5 cm method, its accuracy (mean distance from target) has yet to be determined(2).

Here, we propose a modest simplification of the original technique(8): in practice, full triangulation is not necessary. Two wires (typically the 2 shortest distances, e.g. left tragus and nasion) are sufficient to localize the target. Three wires are necessary in classic triangulation problems because the intersection of two circles yields two points, an ambiguity typically resolved by a circle centered on a third point. In this case, there is no ambiguity because the second intersection of the two wires will be in a nonsensical anatomical location.

A limitation on this result is the use of suboptimal human generated measurements for nearest cortical distance. Future studies could employ more sophisticated human measurement algorithm or automated nearest neighbor algorithm. Studies directly testing the 2-wire or 3-wire triangulation method in conjunction with virtual stereotaxic system will give the true reliability of this simple method.

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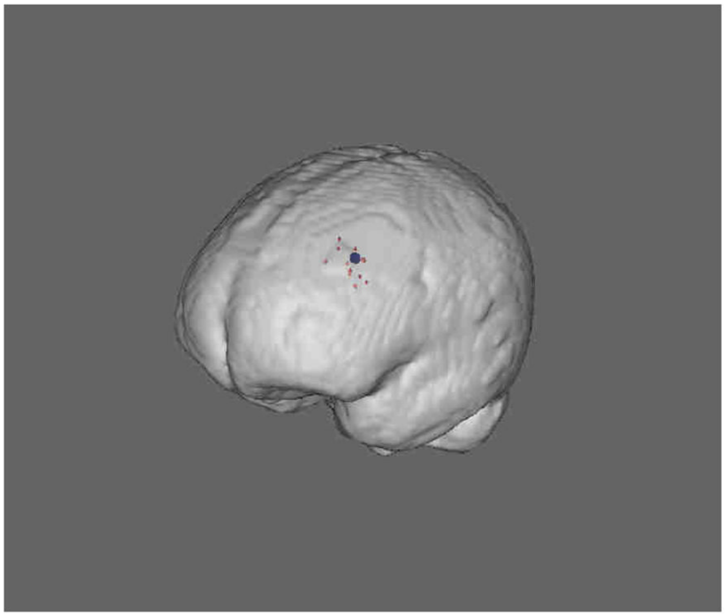

Figure 1.
Actual stimulation targets in MNI-152 space (red) superimposed over the fixed cortical target (blue).