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Intra- and Intersubject Reliability of Abductor Pollicis Brevis Muscle Motor Map Characteristics With Transcranial Magnetic Stimulation

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Abstract

Objective—To determine consistency in motor maps of the abductor pollicis brevis (APB) muscle using transcranial magnetic stimulation (TMS) with conventional and close-spaced surface electrode recording placements.

Design—Nonrandom convenience sample.

Setting—TMS laboratory.

Participants—Eleven participants without any known neurologic disorders.

Interventions—The left hemisphere of right-hand-dominant subjects was mapped using TMS at each of 2 sessions, separated by 1 to 8 weeks.

Main Outcome Measures—Measurements at each session included the resting motor threshold, active site locations and average motor response amplitude for active sites, normalized map volume, and center of gravity (COG) for both electrode array configurations.

Results—The normalized map volume was larger for the conventional electrode placement than for the close electrode placement (4.23cm^2 vs 3.44cm^2 , $P=.010$). Resting motor threshold was higher for the close-spaced than for the conventional-spaced electrodes (48.36% vs 46.59% , $P=.028$). No statistical difference was found between sessions and within electrode placements for the normalized map volume, for resting motor threshold, or for the mean motor amplitude of the most active site for each map. No statistical difference was observed for the COG distance between electrode placements.

Conclusions—This study revealed differences between close-spaced and conventional-spaced surface electrode placement for TMS motor map volumes and for resting motor thresholds. The motor maps for the APB muscle were reliably reproducible between sessions for each electrode array.

Keywords

Electrodes; Electromagnetics; Rehabilitation; Reliability and validity

Transcranial magnetic stimulation (TMS) is a noninvasive technique that can be used to map the motor cortex. TMS involves directing an electric current through a hand-held, copper-stimulating coil, with the consequent production of a transient magnetic field. When held over the scalp, the rapidly changing magnetic field induces a small electric current in underlying brain tissue, which produces a depolarization of nerve cells that is transmitted via the corticospinal tract to contralateral peripheral muscles where a motor response can be recorded with surface electrodes.¹ As an evaluative tool, TMS motor mapping is important because the approach can provide indexes of cortical change after an insult to the brain.² A more detailed discussion on the use of TMS to assess cortical plasticity has been provided elsewhere.³

One area of concern that has not been examined in creating accurate motor maps with TMS is the placement of the surface recording electrodes over the muscle to be examined. Traditionally, nerve conduction studies have been performed with the active electrode over the muscle belly and the reference electrode over an electrically inactive site distal to the recording electrode. The rationale for this approach is to establish a reference away from active tissues to reduce volume-conducted potentials but close enough to minimize environmental noise. If the electrodes are too close together, they may become electrically active at the same time, resulting in the recording of a potential with a lower amplitude than normal. This would inaccurately imply some damage and axonal loss to the nerve because the amplitude of a potential is generally accepted as a measure of the functional axons in a nerve.⁴ In conducting TMS mapping studies, there is a concern that placement of surface electrodes using conventional distances will result in recording electric activity from an area that encompasses many muscles. This approach inherently negates the idea of mapping specific muscles with magnetic cortical stimulation because uncertainty might exist over how to relate changes in response characteristics to changes in actual motor cortical representation of either muscles or movements subsumed by an individual muscle.

TMS motor maps have been shown to be reliably reproduced between hemispheres within healthy subjects and over time.^{5–10} Few studies have examined the intersubject variability in maps generated for specific muscles over multiple recording sessions in healthy subjects or in those with neuropathology, irrespective of the recording electrode configuration. Before TMS mapping can be used as a tool for quantifying cortical organization or reorganization after any type of intervention, the reliability of these maps needs to be more extensively studied.

This study examined inter- and intrasubject reliability of TMS motor maps in able-bodied subjects, mapping the abductor pollicis brevis (APB) muscle using paired electrode placements that were closer together and, therefore, more specific for the given muscle. This approach was contrasted with the motor maps created with conventional electrode placements studied thus far.

METHODS

Our study used a nonrandom sampling of normal participants. The reliability of the motor maps for the APB entailed motor mapping of the left hemisphere in right-hand-dominant subjects during 2 sessions for each participant. The median interval between sessions was 27.5 days (range, 5–64d).

Eleven healthy participants (7 men, 4 women), between the ages of 20 and 60 years and without any known neurologic disorders, were actively recruited by an investigator. They all gave written informed consent to participate in the study, which was previously approved by the institutional review board IRB. The IRB supported the contention that administration of

TMS and procedures for measuring motor evoked potentials (MEPs) are safe and well tolerated.¹¹

Participants completed a questionnaire including date of birth, hand preference for a variety of common tasks, and medical history including use of stimulant or antidepressant medications. Participants were excluded from the study if there was any history of metal on or in the brain (eg, aneurysmal clip), epilepsy, or any known neurologic disorder.

A complete description of the methodology has been provided elsewhere.¹⁰ In brief, a tight-fitting cap with a 1-cm² plotted grid was placed on the heads of participants, so that the stimulating coil position could be accurately determined. Measurements were taken from the vertex to the nasion,inion, and pretragus of both ears, using the vertex as 0,0 coordinate, to assure accurate placement of the cap for each participant and session. The participant was seated in a relaxed position with pillows placed under the forearms and hands.

To elicit valid motor responses, participants were required to be alert but relaxed. Baseline muscle activity was monitored using surface electromyography with audio amplification, to identify prestimulus activation of the APB. Such preactivation has been shown to produce an enlargement of motor maps.¹² Results from other studies^{13,14} have revealed a skewing of the motor map if the participant's level of consciousness and state of relaxation differed from session to session.

During each data-collection session, a manual muscle test was performed, to isolate the ABP for optimal determination of the electrode placements.¹⁵ The skin surface over the APB was abraded with Lemon Prep^a and alcohol until an erythemic response appeared. Recording electrodes^b (7×4mm) were placed on the skin over the APB muscle bellies with their centers approximately 1.5cm apart for the close-spaced electrodes and 6cm for the conventional (wide-spaced) electrodes. A ground electrode was applied ipsilaterally around the circumference of the elbow joint. Skin impedance between reference electrodes and between each reference electrode and the ground were kept below 2kΩ and below 20kΩ, respectively. The investigator holding the TMS coil wore a ground electrode to further reduce signal interference.

The figure-of-eight coil was positioned at 0° in the sagittal plane with the handle oriented posteriorly. The stimulating coil was systematically moved over the scalp, and the motor evoked response was plotted after stimulation of each relevant grid location. The motor-evoked response was determined to be positive if the peak-to-peak amplitude was 50μV or higher. The grid position that elicited the maximal motor potential amplitude with the lowest stimulation intensity in 5 of 10 trials was defined as the "hotspot." The stimulation intensity at the hotspot was defined as the resting motor threshold.

Cortical mapping proceeded at 10% above the resting motor threshold. Grid locations were considered active if at least 5 of 10 stimuli elicited responses that were 50μV or higher. Mapping started at the hotspot location. Subsequently, cortical sites surrounding the hotspot were stimulated. Active sites were identified, and mapping was considered complete when locations adjacent to the active sites were identified as nonreactive, by demonstrating less than 5 of 10 positive responses. The exact mapping procedure was performed for both close-spaced and wide-spaced electrode placements, for each session and each participant. At each session, measurements included the resting motor threshold, hotspot and active site

^aLemon Prep; Faith Medical Inc, 8585 County Rd 133, Steedman, MO 65077.

^bAdhesive disposable surface electrodes; Medtronic Inc, 710 Medtronic Pkwy, Minneapolis, MN 55432-5604.

locations, average motor response amplitude for hotspot and active sites, and the area of the map for conventional and close-spaced electrode placements.

Analysis of the data collected entailed normalization of the motor potential amplitudes obtained to allow comparisons across individuals and across sessions. Normalization of mean MEP amplitudes (nMEP) was completed for all active sites for each mapping session, electrode array, and participant by dividing the mean amplitudes by the maximum mean amplitude. The normalized map volume (nMV) was calculated as a summation of all the nMEPs. The x and y coordinates for each active site were multiplied by the nMEP ($x \times \text{nMEP}$, $y \times \text{nMEP}$), and the sum of all values was calculated respectively. The amplitude-weighted center of gravity (COG) x coordinate was calculated by $\sum x \times \text{nMEP} / \text{nMV}$, and the COG y coordinate was calculated by $\sum y \times \text{nMEP} / \text{nMV}$.¹⁶

Univariate analysis of repeated measures requires the assumption of sphericity. As a conservative procedure to protect against false positives, univariate analyses were therefore conducted with corrected degrees of freedom using the Greenhouse-Geisser correction.¹⁷ A 2-way repeated-measures analysis of variance (ANOVA) was used to explore the difference between sessions and the interaction within the participants for the following variables: resting motor threshold, nMV, and average MEP amplitude for the hotspot. A t test was used to assess the difference between sessions and within participants for the hotspot and COG distances. For all statistical tests, α was set at equal to .05.

RESULTS

Table 1 reveals significant main effects for the nMV and resting motor thresholds between electrode placements. No statistically significant differences were observed between electrode configurations for the mean hotspot MEP amplitude.

There were no differences between sessions and within electrode placements for the mean hotspot MEP ($P=.852$, $P=.866$), nMV ($P=.517$, $P=.307$), or resting motor threshold ($P=.798$, $P=.658$). The nMV was larger for the wide-spaced electrode placement than for the close-spaced array (fig 1). Motor thresholds were higher for the close-spaced electrodes (fig 2).

The COG remained relatively consistent during the 2 sessions for both electrode configurations (fig 3). The mean COG and hotspot movement during 2 sessions was the same (.999cm) for the wide-spaced electrodes. The average COG and hotspot movement was 1.016cm and .968cm, respectively, for the close-spaced array. This mean difference between the electrode placements was .016cm for the COG and .022cm for the hotspot. No difference was found for the movement of the COG and the hotspot location between electrode placements ($P=.954$, $P=.949$, respectively).

DISCUSSION

This study found a significant difference in 2 specific TMS mapping parameters when using 2 different electrode configurations, although there was no difference in COG. Consistent with other findings,^{5–10} TMS motor maps for the APB were reliably reproducible within subjects between sessions for both close- and wide-spaced electrode configurations.

The fact that the nMVs were larger with the wide-spaced electrode array than with the close-spaced array could be explained by the fact that the wide-spaced array spans a larger surface area of the hand than the close-spaced array and may convey motor responses from more than just the APB muscle. Although the close-spaced electrode placement does overlie the flexor pollicis brevis and opponens pollicis in addition to the APB, it may be a more specific representation of the APB. This observation is important if clinicians want to provide an

accurate account of the motor map for a particular muscle. It could be argued that mapping individual muscles is not important. However, certain muscles have a larger functional significance in a clinical disorder, such as stroke. If one uses cortical maps to determine motor reorganization after a stroke, clearly targeting specific muscles and examining changes in their map characteristics may have implications for the value of a therapeutic intervention. Thus, one would like to optimally delineate thumb abduction from total thenar muscle motion that could be subsumed in wide-spaced recordings, because the latter may overestimate the change in cortical map size attributable to inappropriate recruitment of thumb adductor and flexor contributions.³

Measures of cortical reorganization and map volume have been studied, and map volume has been shown to be a reliable parameter for measuring cortical organization.^{12,18–20} Thick-broom et al¹⁴ examined the possibility that map area is determined by current spread from the magnetic coil and does not necessarily provide a true representation of the motor cortical region projecting to a particular muscle. However, our data indicate that there is a difference in the map volume as a function of electrode placements, even if there may be some current spread from the magnetic coil.

Resting motor thresholds were found to be higher for the close-spaced electrode placement than for the wide-spaced placement. This difference could be expected based on the observation that we were targeting a more specific area of the cortex, which required a more intense stimulus to evoke a response. Resting motor thresholds have been reported to be higher for proximal muscles of the upper extremity than for distal ones,^{16,21} perhaps because of the larger muscle mass and/or area of the proximal muscles of the upper extremity. If this observation is true and a wide-spaced electrode configuration does in fact record more muscle mass and area than a close-spaced array, one may expect to see a higher resting motor threshold for the wide-spaced electrodes. Perhaps muscle mass and area are not the determinate variables involved in resting motor threshold levels, but this may warrant further investigation. Our findings on the reliability of resting motor threshold across sessions and within electrode placements are consistent with other studies. Wassermann²² examined resting motor threshold in able-bodied participants and found significant variability between subjects. However, no significant change was found within subjects (n=19) studied across 3 sessions.

The fact that the COG and hotspot distances did not differ between close- and wide-spaced electrode placements across the 2 sessions suggests that the center of excitable area does not change, whereas the map volume varies between electrode placements. Boroojerdi et al²³ found that the COG is an accurate estimation of the location of the muscle representation in the motor cortex when using functional magnetic resonance imaging and recording activity from the first dorsal interosseus, APB, and abductor digiti minimi. The COG has also been used to document cortical reorganization after an intervention reflected in a shift in location.¹⁹ Miranda et al²⁴ demonstrated that the COG was reliably reproduced across mapping sessions within $\pm 3\text{mm}$. Therefore, the COG is an important parameter when analyzing muscle representation in the motor cortex.

Our data did not reveal any differences of the hotspot MEP amplitude between electrode placements across sessions or within electrode placements. By definition, motor mapping, measuring either map volume or COG, is a function of the MEP amplitudes recorded with surface electrodes. Therefore, MEP amplitude reliability is an essential parameter when comparing motor maps of different electrode configurations or muscles of the extremities. Although MEP amplitudes have been shown to vary in size, Thickbroom et al¹³ demonstrated that motor maps are reproducible despite this intrinsic variability. Because the hotspot location was determined to be the most excitable area of the cortex for the APB, we

did not expect this to change in amplitude over time. Liepert et al¹⁹ demonstrated increased MEP amplitudes after constraint-induced therapy in stroke patients, but we did not perform interventions between our recording sessions. The fact that there was no difference between electrode placements is compatible with our observation that the hotspot distance did not differ between electrode arrays.

In our study, several participants had difficulty relaxing completely during the motor mapping, which contributed to prestimulus contraction of the APB. Kiers et al²⁵ examined the effects of stimulus intensity, coil size, mental alertness, and prestimulus muscle contraction on the variability of MEP amplitudes in healthy participants and found decreased variability with increased stimulus intensity and prestimulus muscle contraction. Mental alertness did not significantly alter variability. We used a constant stimulus intensity for each mapping procedure and recorded the motor responses with the muscle at rest. Wilson et al²⁶ showed significant medial displacement of motor maps during muscle contraction (mean, 6mm) compared with maps with the muscle at rest. Prestimulus contraction also increases map size associated with increased MEP amplitudes.^{8,21,27,28} However, Cohen et al^{29,30} found that activating the target muscle does not increase map size. Despite the discrepancies in the literature on the relevance of prestimulus activation, we attempted to eliminate any variability that could be imposed on our data in 2 ways. First, we discontinued recording for several minutes, to allow the participant to stretch and reposition the hand on the pillow when prestimulus activation was observed. The recording session resumed when no muscle activity was observed visually on the monitor and with audio amplification of surface electromyography signals. Furthermore, during data analysis, those responses that exhibited any prestimulus activation were excluded, thus potentially skewing the data.

Occasionally, there was some difficulty in lowering the skin impedance to less than 10k Ω . We found that higher impedances resulted in an extended stimulus artifact duration riding into the response window (at $\approx$ 20ms). Although infrequent, this occurrence impaired accurate measurement of the MEP amplitude. We found that only approximately 3% of all positive responses at the active sites exhibited this extended stimulus artifact and these responses were eliminated on post hoc analyses. This resulted in the averaging of fewer potentials for certain active sites to determine the average MEP amplitude, which could potentially have skewed the data. Last, every effort was made to assure accurate positioning (0° in the sagittal plane) of the magnetic coil during mapping. This consideration is important, because Mills³¹ and Pascual-Leone³² and colleagues found larger MEP amplitudes with a coil orientation of approximately 50° to the sagittal plane (perpendicular to the central sulcus). In most cases, the same experimenter operated the stimulator during both sessions, to reduce the potential for coil positioning errors. However, in fewer than 10% of the experiments, the investigator holding the magnetic coil was different for a given subject or session.

CONCLUSIONS

This study is the first to examine the role of recording electrode positioning and reliability with TMS motor maps for the APB muscle. We found that the map volume and resting motor threshold differed for the close- and wide-spaced electrode arrays, whereas motor maps for the APB muscle were reliably reproducible between sessions for each electrode array. These data reinforce the need to examine carefully factors contributing to accuracy in cortical mapping for specific muscles. The implications for future research and examination of cortical reorganization for functionally relevant muscles after a brain insult are important because such maps may link measures of plasticity with physical or pharmacologic rehabilitative interventions.

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Fig 1. Mean nMV (in cm²) and standard deviation (SD) bars for close-spaced and wide-spaced electrode configurations across sessions.

Fig 2. Mean resting motor threshold (% stimulator output) and SD bars for close-spaced electrodes and wide-spaced electrode configurations across sessions.

Fig 3. COG movement (in centimeters) across 2 sessions for each participant and electrode array, using 2-dimensional view of left hemisphere. COG was calculated using mean MEP amplitudes shown for the active sites only. The 0,0 coordinate represents the location of the vertex. The x axis represents the lateromedial plane, and the y axis represents the posteroanterior plane in 1-cm^2 grids.

Two-Way Repeated-Measures ANOVA Comparing Mean Values for nMV, Hotspot MEP Amplitude, and Resting Motor Threshold for Both Electrode Configurations and Each Session

Table 1

Measures	Close-Spaced		Wide-Spaced		P*
	Session 1	Session 2	Session 1	Session 2	
nMV (cm ²)	3.03±0.97	3.85±1.09	4.41±1.80	4.06±1.31	.009
Hotspot MEP amplitude (V)	0.28±0.35	0.30±0.21	0.27±0.23	0.27±0.18	.764
Resting motor threshold (% stim output)	48.46±14.07	48.27±1.03	46.18±12.55	47.00±12.21	.028

NOTE. Values are mean ± standard deviation.

* P-values reflect a comparison between the close- and wide-spaced electrode configurations.