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Variability of motor cortical excitability using a novel mapping procedure

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Abstract

The purpose of this study was to assess the reliability of a novel TMS motor cortex mapping procedure. The procedure was designed to take less time and be more clinically useful by delivering fewer MEPS over fewer skull locations. Resting motor evoked potentials (MEPs) were recorded from the first dorsal interosseus muscle of 6 individuals over a fixed 15-point grid. Mean MEP amplitudes, map center of gravity (CoG), and stimulus-response characteristics were assessed before and after a 30-minute rest session. As a novel feature, subregions of the map were analyzed for regions of highest test-retest reliability for use as a global measure of cortical excitability. Mean MEP amplitudes between sessions were highly reliable (ICC = 0.90–0.92). Reproducibility of MEPs was highest along an axis approximately 45° to the nasion-inion. Stimulus response MEP amplitudes showed moderate to high reliability (ICC 0.54–0.95). Mean CoG shift between sessions was 2.79 ± 1.2 mm. This mapping procedure is reliable and allows efficient assessment of motor cortex excitability.

Keywords

Transcranial magnetic stimulation; Motor evoked potentials; Reliability; Mapping; motor cortex

1. Introduction

Transcranial magnetic stimulation (TMS) offers a safe, non-invasive technique (Hallett, 2000; Rossi et al., 2009) to quantify modulations in the excitability or topography of muscle or movement representations in the primary motor cortex (M1) that accompany changes in motor behavior (Cohen et al., 1993; Donoghue, 1995; Sanes and Donoghue, 2000). With novel motor or sensory inputs, cortical representations undergo significant task-dependent facilitation of motor evoked potential (MEP) amplitude (Jensen et al., 2005), potentiation of TMS input-output characteristics (Jensen et al., 2005; Lotze et al., 2003), or movement of the amplitude-weighted locus of MEP activity, or center of gravity (CoG) (Liepert et al., 2000a). Typically, the cortical representations are spatially distributed and show

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considerable overlap with adjacent muscles such that selective stimulation of individual muscles in the upper extremity can be difficult (Beisteiner et al., 2001; Donoghue et al., 1992; Schieber, 2001; Wilson et al., 1993). As such, single-point measurement of cortical excitability (frequently at the motor hotspot) may be insufficient to adequately characterize excitability changes across the distribution, most notably directionally-specific expansions or modulations. Comprehensive mapping of M1 offers utility to investigate spatial variation in excitability or reorganization of the distribution in response to therapeutic interventions such as skill learning, exercise, or manipulation of sensory input.

M1 mapping has been shown to reliably quantify cortical modulations in response to motor skill learning in healthy individuals (Pascual-Leone et al., 1995; Pascual-Leone and Torres, 1993) and those with central nervous system lesions (Liepert et al., 2000a; Liepert et al., 2000b; Perez and Cohen, 2009). In many cases, extensive systematic mapping procedures may be time consuming, lasting potentially as long as 45–60 minutes (Kleim et al., 2007), such that modulation of cortical excitability induced by experimental or clinical interventions may be inadequately characterized if mapping durations outlast acute effects of the intervention. Moreover, fluctuations in subject comfort or alertness may increase MEP variability during long duration testing (Ziemann et al., 1996). For those reasons, we designed a short-duration cortical mapping and recruitment procedure based on a fixed 15-point grid for mapping the first dorsal interosseus (FDI) muscle in the hand. We sought a procedure that would rapidly and reliably measure acute changes in MEP excitability, while minimizing potential for subject fatigue or fluctuations in alertness. We also investigated whether certain regions of the cortical map might show greater reliability, and, as such, show potential as a global marker of excitability changes measured during or after interventions.

Previous studies report moderate to good between session reliability of MEP amplitude at the FDI motor hotspot ($ICC = 0.6–0.81$) separated by 24 hours (Kamen, 2004). Similar between-session reliability was observed in stimulus-response recruitment curve slope ($ICC = 0.82$) and in the mediolateral coordinate of the CoG ($ICC = 0.85$) when tested over a two week period, though anterior-posterior coordinate reliability was low ($ICC = 0.38$) (Kamen, 2004; Malcolm et al., 2006). Reproducibility of the CoG in hand muscle representations is generally within 1–3 mm (Malcolm et al., 2006; Miranda et al., 1997; Wolf et al., 2004). One recent study used a 15-point (3×5 cm) grid centered at the motor hotspot to derive cortical maps and CoG modulation in the upper extremity representation in subjects with hand amputation; however, the reliability of the method for muscles in the hand was not established (Gagne et al., 2011). As with any new methodology, determining reliability is necessary to establish the clinical utility of the measures. Hence, the purpose of this study was to determine between-session reliability of the MEP amplitude, stimulus-response recruitment curve, and map CoG of the FDI cortical representation.

2. Methods

2.1. Subjects

Six healthy volunteers (1 female), aged 19–39 (mean 26.8 ± 8.0) years participated in the study. Exclusion criteria were history of neurological or cardiovascular disorders, history of seizures, implanted electrodes or pacemakers, any non-dental metal in the head, or long-term specialized use of the hands such as playing a musical instrument (Rosenkranz et al., 2007). All subjects were right handed. Each subject completed a safety inventory prior to participation to screen for potential contraindications to TMS (Keel et al., 2001) and provided written informed consent in accordance with the University of Iowa Institutional Review Board. Subjects refrained from exhaustive exercise and consumption of alcohol and caffeine in the 24 hours prior to the experimental session.

2.2. Data Collection

Motor evoked potentials were recorded from the first dorsal interosseus (FDI) muscle of the left hand with bipolar Ag-AgCl electrodes (8mm diameter with 20mm inter-electrode distance). The skin overlying the muscle was abraded with sandpaper and cleaned with alcohol to minimize skin impedance. The common ground electrode was affixed to the anterior tibia of the ipsilateral leg. EMG data were amplified (1–5k), filtered (20–4000Hz), digitally sampled at 2 KHz, and stored on computer for offline analysis. 100 ms of pre-stimulation activity and 150 ms of post stimulation activity were recorded. MEP amplitude was measured as the peak-to-peak amplitude taken from a time window 20–50ms after the magnetic stimulus pulse onset. Trials in which active contraction contaminated the MEP were omitted. EMG data were digitized and analyzed using Datapac 2K2 ver. 3.18 (Run Technologies Co., CA). For analysis, MEPs were normalized to the mean maximal voluntary isometric contraction (MVC) amplitude. Voluntary EMG was rectified and band pass filtered (10–200 Hz). EMG amplitude was calculated as the mean RMS amplitude of the rectified, filtered signal taken from a 1000 ms window centered at the MVC force peak.

Stimulation of the right motor cortex was delivered by a Magstim 200² stimulator (Magstim Company Ltd., Whitland, Dyfed, UK) equipped with a 70 mm diameter figure-of-eight coil. The coil was held tangentially to the skull surface at a 45° angle to the sagittal plane with the handle oriented posterolaterally to create a posterior-to-anterior current flow over the cortical surface (Brasil-Neto et al., 1992; Werhahn et al., 1994). Starting approximately 2 cm anterior and 4 cm lateral to the skull vertex, the coil was moved in 0.5–1 cm increments systematically across the anterolateral scalp surface until the site eliciting the largest average MEP in the resting FDI (stimulation intensity equal to 50–60% maximal stimulator output) was located (motor “hotspot”). The optimal coil orientation for eliciting MEPs was recorded and monitored by a Polaris infrared 3-D stereotactic positional tracking camera (Northern Digital, Inc., Waterloo, Ontario, Canada) with respect to a 3-D head reference marker affixed to the subject’s forehead and digitized to four anatomical landmarks (ear tragic, tip of nose, and skull vertex).

2.2.1. Justification of Mapping Grid Design—The map geometry was chosen to measure cortical motor excitability over the FDI representation with emphasis along the approximate longitudinal axis of the central sulcus (Figure 1), while minimizing focal stimulation over the primary sensory cortex located approximately 3 cm posterior to the hand motor hotspot (Koch et al., 2006) or the lateral premotor cortex, located approximately 2.5–3 cm anterior to the FDI motor hotspot (Gerschlagel et al., 2001). Comprehensive mapping often includes recording all active sites producing MEPs over a somatic representation (Butler et al., 2005; Cicinelli et al., 1997; Corneal et al., 2005; Liepert et al., 2000b) though may involve hundreds of stimulation pulses. Fixed area mapping grids have been used estimate changes in cortical representation range in size from 3 × 3 cm (Jones-Lush et al., 2010), 5 × 5 cm (Malcolm et al., 2006) to 7 × 7 cm (Classen et al., 1998). Wilson and colleagues found the majority of activity in abductor pollicis brevis muscle occurred within a 5 × 7 grid up to 2–3 cm from the hotspot (Wilson et al., 1993). We chose 5 × 7 cm grid dimensions (15 points) with maximum distance of 3 cm from the hotspot as an acceptable representative sampling of active MEP sites, while still maintaining a clinically feasible duration of 12–15 minutes to collect 75 MEPs.

2.2.2. Cortical Mapping—FDI motor maps were created by applying 5 consecutive stimuli at each point of the 15-point grid centered at the FDI hotspot for each subject (Figure 1). Stimuli were delivered at 120% RMT with stimulation frequency 0.1 Hz, starting with the hotspot. The order of stimulation over the remaining grid points was randomized. Stimulation was limited to 5 pulses at 15 points to achieve session durations feasible for

clinical use yet allow characterization of potential brief excitation modulations. Pilot data of cortical mapping showed no significant differences in mean MEP amplitude of individual grid points whether derived from 5 or 10 stimuli, thus 5 stimuli were used to minimize time necessary for the procedure. Moreover, recruitment curves did not differ when using 20% intensity increments versus 10% increments to derive the curve.

2.2.3. Stimulus-Response MEP Measurements—Stimulus-response measurements were measured via five stimuli delivered per intensity at 80, 100, 120, 140, and 160% RMT. Stimuli were delivered in pseudorandom order at a frequency 0.1 Hz. The mean amplitude of the 5 MEP's were calculated at each grid map point. The change from the mean of measurement 1 (pre) to the mean of measurement 2 (post) was calculated for each subject as the % change (measurement 1 – measurement 2/measurement 1). A MEP amplitude ratio was calculated as the ratio of the mean MEP amplitudes for measurement 2 (post) divided by measurement 1 (pre) to best illustrate the second MEP measurement relative to the first MEP measurement.

2.2.4. Center of Gravity Measurements—The CoG of the motor map was derived from the mapping grid. The motor map CoG X-coordinate was calculated by $\bar{X} = \sum (x \cdot z) / \sum z$ and the Y-coordinate by $\bar{Y} = \sum (y \cdot z) / \sum z$. $\bar{X}$ and $\bar{Y}$ are expressed in centimeters in relation to the motor hotspot, while Z represents the mean MEP peak-to-peak amplitude at each grid point. The Euclidian equation was applied to determine the mean scalar distance the CoG shifted between sessions.

2.3. Experimental Procedures

Subjects were seated comfortably in a semi-reclined position with the head supported on a headrest. The left shoulder was flexed and abducted to approximately 30°, with the hand resting palm down on a table. The hand was positioned with the index finger in neutral abduction, supported in a modeling clay splint custom-molded to each subject's hand. Following identification of the FDI hotspot, we determined the resting motor threshold (RMT) starting at suprathreshold stimulus intensity, then decreasing the intensity in 5% increments of maximal stimulator output until the stimulus intensity became sub-threshold (Rossini et al., 1994). RMT was defined as the minimum stimulator intensity eliciting MEP amplitude of 50µV in at least 4 of 8 consecutive trials. The mapping and recruitment curve procedures were performed consecutively and then repeated using stimulus intensities identical to the first session after a 30-minute rest interval. Between sessions, the investigator marked the location of the camera head reference marker and EMG electrode and removed them from the subject. Electrophysiological reliability when removing the marker and electrode was of methodological interest for future studies necessitating removal during therapeutic interventions. Subjects sat quietly in a separate chair during the rest interval. Prior to the second mapping session, the electrode and marker were reapplied. The position of the head reference marker was re-digitized to the four anatomical landmarks on the subject's head to ensure accurate replacement. The total re-digitizing error across 4 digitizing points after reapplication of the head reference marker was 1.14 ± 0.6 mm. Pilot data measuring re-digitizing error without removal of the reference marker from the head was 1.18 ± 0.8 mm.

2.4. Data Analysis

The relative reliability of the TMS-related measurements was analyzed using the intraclass correlation coefficient (ICC) based on a one-way repeated measures analysis of variance (ANOVA). Grid map test-retest reliability and stimulus-response recruitment were analyzed using paired t-tests and Pearson correlation coefficients to assess consistency and average

agreement between sessions. Stability of the CoG between sessions was testing using the ICC. For all tests, the alpha level was set to 0.05.

3. Results

3.1. Motor Cortex Mapping

Figure 2 shows the change in mean MEP amplitude at each map grid point between-sessions expressed as a ratio of the repeated measure to baseline measure. The percent change in amplitude of individual grid points ranged from 0.81–2.75). Motor map mean MEP amplitude of the 15 combined grid points did not differ significantly between sessions (1.38 ± 1.07 mV vs. 1.21 ± 0.92 mV; $P=0.29$). Grid points along the grid abscissa showed the smallest change in normalized MEP amplitude (ratio 0.81 ± 0.45 to 1.25 ± 0.57). Grid points N1, N2, NE, and SE showed the largest change in amplitude and largest variation in MEP amplitude between sessions (ratio 1.71 ± 2.18 to 2.75 ± 2.87).

We analyzed subsets of points of the grid to investigate whether different topographies of the map showed greater test-retest reliability, and thus greater sensitivity to detect change during intervention trials (Figure 3). Grid subsets included the center 3×3 matrix of 9 points directly adjacent to (and including) the FDI hotspot, points along the grid abscissa (W3 E3, 7 points), and central points on the abscissa (W2 E2, 5 points). Comparison of the reliability of the mean amplitude of the grid is shown in Table 1. The mean motor map MEP amplitude decreased during the second session in all combinations (–11.0 to –15.1%), though no grid subsets differed significantly between sessions. Mean MEP amplitudes showed significant correlations in each subset (0.82–0.87). ICC coefficients ranged from 0.90–0.92 indicating high test-retest reliability.

3.2. Stimulus-Response Recruitment

Ratios of MEP amplitude derived at the motor hotspot during the recruitment procedure are shown in Figure 3. Mean MEP amplitude by subject decreased between sessions for 3 of the 4 intensities (see Table 2); however, none of the differences reached statistical significance. MEP amplitude between sessions was significantly correlated at 100, 140, and 160 %RMT ($r = 0.83, 0.94$, and 0.93 respectively, $P < 0.05$), but not at 120% RMT ($r = 0.44$, $P = 0.38$). Stimulation amplitudes of 100, 140, and 160% RMT showed high between-session reliability (ICC = 0.88–0.95) while reliability at 120% RMT was moderate (ICC = 0.54).

3.3. Center of Gravity

Graphical representation of CoG movement between sessions is shown in Figure 4. The mean distance of CoG shift was 2.79 ± 1.3 mm. The mean scalar distance of the x- and y-coordinates was 1.86 ± 1.2 and 1.90 ± 1.1 mm, respectively. The ICC coefficients of the x- and y-coordinates were 0.91 and 0.39, respectively, indicating high reliability between sessions for CoG position along the grid abscissa, but low reliability for the ordinal position.

4. Discussion

The use of transcranial magnetic stimulation to study plasticity parameters is becoming increasingly widespread. Hand and forearm muscles are easily accessible for studying acute and chronic adaptations of M1 representation in individuals with and without neurological lesions. A primary goal of rehabilitation specialists is to evaluate and design activity-based intervention strategies that induce or enhance beneficial neuroplastic processes. As such, methods to assess adaptations that are both reliable and clinically feasible are necessary. Numerous mapping protocols have been shown to reliably map hand musculature using TMS (Cicinelli et al., 1997; Miranda et al., 1997; Mortiffee et al., 1994; Uy et al., 2002;

Wilson et al., 1993); however, methods vary widely in temporal and spatial assessment. Accordingly, the main purpose of this study was to investigate the test-retest reliability of a short-duration mapping procedure using a fixed grid for estimating acute changes in cortical excitability of a representative muscle in the hand.

The main findings of this study were: 1) FDI mean MEP amplitude was highly reliable between sessions across the mapping grid. Grid points distant to the hotspot on the ordinal axis showed the greatest MEP amplitude variability between sessions. 2) Recruitment curves showed no significant difference in curve shape between sessions. 3) The location of the grid map CoG was highly stable across sessions. The x-coordinate showed greater between-session reliability than the y-coordinate.

Motor Mapping

The motor cortex is organized in terms of movements associated with complex interactions of different muscles under the influence of multiple brain centers. Thus, it is not unreasonable to expect that reproducibility may vary at different points on map topography. While mean MEP amplitude of the entire 15-point map was highly reproducible, the ordinal periphery of the map showed greater percent change in amplitude than those points situated closer to the estimated axis of the central sulcus. Mortifee et al. (Mortifee et al., 1994) measured lower intersession coefficients of variation in MEP amplitude primarily (though not exclusively) along the periphery of the adductor pollicis brevis and abductor digiti minimi somatotopic motor maps. Most prior mapping studies have measured the area of the map as the number of points at which a response was evoked in the target muscle (Miranda et al., 1997; Mortifee et al., 1994; Uy et al., 2002). We kept the area of the motor map fixed in the present study in the interest of session brevity and to minimize potential variability at the periphery of the map. One limitation of constructing maps using fixed grids is that some active cortical sites may not be stimulated, thus underestimating map dimensions near active but unstimulated sites. Cicinelli and colleagues used a similar model of 11 stimulation sites covering an 8 × 8 cm region of the abductor digiti minimi (ADM) to measure interhemispheric differences in motor representation (Cicinelli et al., 1997). Maximal “hotspot” activity in both hemispheres was centered primarily around 3 adjacent points approximately 2 cm apart. The same group reported greatest MEP activity along a vector corresponding to the central sulcus alignment including “anomalous hot spots” located outside the locus of ADM representation in patients with hemispheric stroke (Traversa et al., 1997). In the thenar and hypothenar eminences, Mortifee et al. noted individual stimulation points that had a low coefficient of reliability (< 25%) intermingled in an apparently random arrangement with stimulating sites that had high coefficients of reliability (> 75%) (Mortifee et al., 1994). The authors presumed that sites with high coefficients of reliability correspond to those parts of the cortical map having the lowest thresholds, citing the reverse relationship between threshold and MEP amplitude. The variable reliability in the present study may then reflect a similar fractionated nature of the FDI distribution.

Though not significantly different, the mean MEP amplitude of the comprehensive map was lower between sessions in 4 of 6 subjects. This may be due in part to greater subject familiarity with the procedure and thus potential less anxiety about the magnetic stimulation during repeat mapping that may influence interindividual variability (Wassermann et al., 2001). At the same time, this finding supports that the injection of magnetic energy during the procedure did not itself increase overall excitability, an important consideration for future studies investigating the effects of therapeutic interventions on cortical excitability. The locations of the grid map that show the least variation were located primarily on the x-axis itself. The current study did not have imaging reference points to verify the orientation of the coil with respect to the central sulcus and motor strip; however, with the 45° oblique

angle of the coil, it is suggested that movement along the ordinal axis represented a movement perpendicular to the primary motor strip.

Stimulus-Response Recruitment

Overall, reliability during the recruitment procedure was high ($ICC = 0.85\text{--}0.92$) with the exception of 120% of resting motor threshold ($ICC = 0.44$, $MEP\ \%change = -36.5\%$). This is in contrast to high measured reliability ($ICC = 0.95$, $MEP\ \%change = -13.5\%$) to MEP acquired at the identical location and intensity during the mapping procedure. It is possible that MEP may have been influenced by the preceding pulses, although intensities during recruitment were presented in pseudorandom order, arguing against an ordering effect. However, given the differences in reliability between the mapping and recruitment procedures, a greater number of stimulus pulses may be necessary to lessen the influence of the natural within-subject variation of the MEPs.

A potential limitation of the mapping protocol in this study is reduced sensitivity to expansion of the motor map. For this reason we measured the stimulus-response characteristics across progressively increasing stimulus intensities. Growth in the map area may be cautiously inferred by the input-output relationship. Ridding and Rothwell observed during acute (ischemic) and chronic (amputation) modulation of upper extremity cortical maps that increases in recruitment curve slope qualitatively mirrored increases in motor map area of the biceps brachii and forearm flexors, suggesting that recruitment curves can be used to detect changes in motor maps. The authors cautioned that while recruitment curves will detect changes in the area of cortical maps, they do not readily detect changes in the distribution of excitability or uneven expansion of the cortical map (Ridding and Rothwell, 1997).

Center of Gravity

The CoG represents the amplitude-weighted center of the motor map. A shift in the CoG position is frequently used to represent functional or architectural reorganization in the motor cortex with skill acquisition (Liepert et al., 2004) or after neurological lesions (Cicinelli et al., 1997). In the present study, the absolute distance of CoG movement was 2.7 mm between sessions, slightly less than prior studies reporting average shifts of 3–4 mm (Miranda et al., 1997; Uy et al., 2002). To examine whether the larger dimensions of the grid along the abscissa compared to the ordinate influenced position of the CoG, we analyzed the shift in CoG position using only the 3×3 stimulation point matrix of points immediately surrounding (and including) the FDI hotspot. The magnitude and direction of the CoG did not differ between the 3×3 matrix and the full 15-point map.

Separate reliability analyses were performed for the CoG x- and y-coordinates. Absolute mean CoG movement was nearly identical between the x- and y-coordinates (1.86 ± 1.2 mm and 1.90 ± 1.1 mm, respectively); however, the x-coordinate location ($ICC = 0.91$) showed high reliability, whereas the Y-coordinate reliability was low ($ICC = 0.39$). It should be emphasized that the y-axis in this study was aligned parallel to the orientation of the coil. The y-coordinate variability may be influenced by the parallel direction of the induced current to a greater degree than in studies reporting the y-axis as parallel to the nasion-inion line. Motor maps are often elongated along the axis of the coil (Wilson et al., 1993), thus the increased variability in MEP amplitude and lower reliability in CoG location in the y-axis may be due in part to the 45° oblique orientation of the coil. The present study benefitted from use of a 3-D tracking camera to monitor coil location and orientation with a high level of precision. In general, coil position error was < 1 mm from the defined stimulation point, and within $1\text{--}2^\circ$ of the original planar orientation. Moreover, reapplication of the head reference marker between sessions introduced no more than 2 mm of spatial error. For this

reason we are confident that the inherent variation in the TMS parameters was not a function of coil position changes that may alter the pool of neuron stimulated during the experiment.

Functional Considerations

The present findings suggest that while variation of individual locations across the somatotopic representation responded differently, group mean parameters were stable between sessions. A novel component of this study was the assessment reliability of different subsets of the motor map to determine whether certain loci or combinations of loci provided a more stable estimate of MEP amplitudes that may be used as a global measure of excitability beyond the use of a single point, yet retain session brevity. Intraclass correlation coefficients of MEP amplitudes were similar between the hotspot, full map, and points along the grid abscissa suggesting that each combination may serve as a reliable estimator of overall excitability. Despite prior reports of increased variation at the periphery of the map {Mortifee, 1994 #130}, the added topography of the full map did not adversely affect reliability of the excitability measures. These findings support the use of comprehensive mapping to elucidate cortical modulations reflected by the entirety of the map. Moreover, low variation in center of gravity locations supports the use of the current methodology to determine directional shift of the locus of excitability within the confines of the motor map. Future studies are necessary to determine the reliability across longer time durations for use in assessment of therapeutic interventions designed to enhance cortical plasticity.

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Highlights

MEP amplitudes were highly reliable using a newly developed technique for examining motor maps.

MEP amplitudes along an axis $\sim 45^\circ$ to the nasion-inion were most reliable.

Stimulus response MEP amplitudes showed moderate to high reliability

Center of Gravity shifts between sessions were minimal

Figure 1.

(A) Two-dimensional diagram of the mapping grid. Stimulation points were spaced at 1 cm intervals with the grid origin centered at the FDI motor hotspot. Grid loci are identified by the cardinal compass point and distance from hotspot. Ordinal axis corresponds to the vertical axis of the TMS coil. (B) Representation of the mapping grid overlying M1. The black reference line corresponds to the grid abscissa aligned along the approximate axis of M1.

Figure 2.

Mean post:pre ratio of MEP amplitudes between sessions across the mapping grid. Grid loci are listed as the cardinal compass point and distance from the FDI motor hotspot (see Figure 1 for reference).

Figure 3.

MEP amplitude post:pre ratios for mapping grid subregions (mean $\pm$ SE). All MEPs during the mapping procedure were obtained at 120% RMT. Ratios of MEP amplitudes during the recruitment procedure are shown by stimulus intensity. All recruitment ratios were obtained at the motor hotspot.

Figure 4.

2-D representation of CoG movement (cm) between sessions for each participant. The COG was calculated using mean MEP amplitude of all 15 grid points of the FDI motor map. Arrows represent the direction of movement between sessions.

Table 1

Reproducibility of motor map and subsets (n = 6)

Grid Subset	MEP %Change	P value	r value	P value	ICC
Full Grid	-11.0	0.13	0.87	0.023 *	0.93
3×3 Center Grid	-15.1	0.10	0.88	0.022 *	0.92
Hotspot	-13.5	0.14	0.94	0.005 *	0.94
W3 E3 X-axis	-13.1	0.31	0.82	0.043 *	0.90
W2 E2 X-axis	-13.0	0.34	0.83	0.040 *	0.90

* indicates significant Pearson correlation

Table 2

Reproducibility of MEP amplitude by recruitment intensity (n = 6)

Recruitment Procedure	Intensity (%RMT)	MEP %Change	P value	r value	P value	ICC
100		1.7	0.95	0.83	0.042 *	0.88
120		-36.5	0.26	0.44	0.384	0.56
140		-14.7	0.27	0.94	0.006 *	0.95
160		-18.0	0.31	0.93	0.007 *	0.92

* indicates significant Pearson correlation