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Reliability for non-invasive somatosensory cortex localization: Implications for pre-surgical mapping

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ABSTRACT

Objectives: In patients with epilepsy or space occupying tumors in cortical regions, surgical resection is often considered as the primary treatment. Pre-surgical neuroimaging can provide a detailed map of pathological and functional cortex, leading to safer surgery. Mapping can be achieved non-invasively using magnetoencephalography (MEG), and is concordant with invasive findings. However, the reliability of MEG mapping between sessions is not well established. The inter-session reliability is an important property in pre-surgical mapping to establish resection margins, but repeated scans are impracticable. The present study sought to quantify the intersession reliability of MEG localization of somatosensory cortex (S1).

Patients and methods: Eighteen healthy individuals underwent MEG sessions on 3 consecutive days. Five participants were excluded due to technical issues during one of the three days. Each session included clinical-style S1 localization using electrical stimuli to each median nerve at sub-motor thresholds. The 35 ms peak of the somatosensory evoked field was used for localizing S1 in each session using a single equivalent current dipole model. Intersession reliability was quantified using two methods. Average Euclidean Distance (AED) quantified the difference in localization between each session and the inter-session mean localization. Session Euclidean Distance (SED) quantified the difference in localization between each pair of sessions.

Results and discussion: Results showed the AED was 4.8 ± 1.9 mm, whereas the SED was 8.3 ± 3.4 mm. While the AED values obtained parallel those reported previously in smaller samples, the SED values were substantially larger.

Conclusion: Clinicians should consider up to an 8 mm confidence interval around the estimated location of S1 based on MEG pre-surgical mapping.

1. Introduction

In patients diagnosed with epilepsy or space occupying tumors, a valid protocol to alleviate symptoms is to resect the damaged cortex or the tissue serving as the focal point for the epileptic seizures. Surgical procedures are considered for those who have disabling impairments due to the nature of the damage, those who are refractory to their medications and those who have medication side effects that alter their quality of life. In order to reduce cognitive and/or motor impairment as a direct outcome of surgery, it is imperative to cause minimal or no damage to the functional cortex surrounding the area that is to be resected. Clinicians elucidate functional cortex, in part, using functional mapping techniques. For use in surgical planning, it is essential that functional mapping is accurate (identified the correct brain area to spare) and reliable (the same result would be found if repeated). The gold standards for mapping are invasive, and include the Wada test [1] and direct cortical stimulation (DCS), both of which are used based on validated accuracy and reliability. As an example, DCS involves implanting electrodes directly onto the patient's brain during an awake craniotomy. Stimulation via the implanted electrodes inhibits areas of

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the cortex while the subject performs specific tasks. If function is affected by the stimulation, then the area is deemed an "area of eloquence", and in-turn is identified as one to spare during surgery.

Non-invasive pre-surgical functional mapping during planning can alleviate some of the challenges associated with invasive options, such as the Wada test and DCS, potentially leading to better patient outcomes. Procedures such as magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and navigated transcranial magnetic stimulation [2] are emerging as viable non-invasive alternatives for pre-surgical mapping [3], Given the invasive nature of procedures like DCS, there are inherent surgical risks with severe health consequences [4]. The DCS procedure also requires compliance from the patient to complete the required tasks under challenging circumstances. This limits the applicability of the procedure to groups with challenges for compliance, such as young children and patients with neurological or cognitive deficits [5]. Furthermore, DCS is usually performed during the respective surgery, which limits the amount of time and individuals available for consulting about DCS findings prior to resection.

In order to impact positively on decisions related to surgical approach and resection margins, non-invasive techniques such as MEG need to demonstrate both a high level of accuracy and intersession reliability. From a clinical perspective, accuracy and reliability are important to ensure that the MEG localization correctly identifies the targeted neural tissue, and that the coordinates provided by the localization would not change if the scan were repeated. This latter feature is important for characterizing the variability associated with the localization technique, as completing multiple sessions of pre-surgical mapping to establish variability is not a viable option in a clinic setting.

The accuracy of MEG for pre-surgical cortical mapping has been established in the primary somatosensory cortex (S1) via comparison to invasive mapping, which is the gold standard mapping method, and by surgical outcome [6,7]. Localization of S1 is a good test case for pre-surgical mapping techniques as robust patterns of activation can be determined in a single patient using MEG and DCS. However, the inter-session reliability (i.e., consistency between sessions) of localization using MEG pre-surgical mapping has not been well examined in past. Quantifying intersession reliability will provide clinicians with an estimate of how much the localization provided by a single MEG scan could differ due to the variability associated with the imaging technique itself, toward establishing critical margins of error during surgery.

Accordingly, the primary objective of this study is to provide a robust measure of the intersession reliability of S1 localization with MEG. Measures of intersession reliability have previously been established, ranging between 2.8 and 7 mm, but only for single participants [6,8]. While both studies established baseline measurements for intersession reliability, there are two issues with this previous work. Firstly, measures of reliability were derived from a single participant, and may not be representative of the larger population. Secondly, the methodology for determining intersession reliability was not described in either report. Owing to these limitations, we have further studied the inter-session reliability of MEG localization to better assess the utility of MEG for pre-surgical mapping.

To achieve our primary objective, the current study seeks to examine intersession reliability of MEG S1 localization in a cohort of individuals using two different approaches to quantify reliability. We anticipate that localization of S1 will be consistent across sessions. Results of the study will increase our understanding of the intersession reliability, and in-turn variability, of localization using MEG, allowing clinicians to make more informed decisions about resection margins during pre-surgical planning.

2. Methods

2.1. Subjects

Eighteen healthy right-handed volunteers participated in the study (10 females; 24.7 ± 3.8 years). All subjects were free of neurological disorder and each provided written, informed consent. Prior to the onset of the study, subjects were screened for compatibility with MEG according to institutional procedure. The Research Ethics Board at the IWK Health Centre approved the study.

2.2. Data acquisition

Neuroimaging data was collected using a 306 channel MEG system (Elekta Neuromag Oy, FL) using standard pre-surgical functional mapping procedures. The vertical and horizontal electrooculogram was also obtained using four electrodes, with one superior and one inferior to the left eye, and one just lateral to the left and right eye, with a ground electrode attached to the collarbone. Additionally, four head position indicator coils were placed on the subject's head; two on the forehead and one on each mastoid process. The positions of the coils, anatomical landmarks, and a 200-point head model were digitized using a Polhemus digitization device (Polhemus Incorporated, Vermont, USA). During scanning, coils were activated continuously to permit tracking of head movement. All data were acquired continuously at a sampling rate of 1500 Hz and a bandwidth of 0.1–500 Hz, and recorded to a file for off-line analysis.

To generate robust activation in S1, percutaneous electrical stimulation was applied to the left and right median nerves at the level of the wrist (DS7A Constant Current Simulator, Digitimer, England). Prior to MEG scanning and for each wrist, stimulator output was increased until a visible twitch of the median innervated thenar muscles was observed. Stimulator output was then reduced until the twitch was no longer visible, but the participant reported a sensory response with each stimulus. Eighty stimuli were then applied to each wrist in random sequence (to a maximum of 4 consecutive stimuli on one side) with an inter-stimulus interval varying between 1 and 2 s. Markers indicating the onset and side (left or right wrist) of each stimulus were acquired with the continuous MEG recording to facilitate event-related analysis. Participants attended three experimental sessions performed at approximately the same time on consecutive days. Data reported was collected as part of a larger study examining neurofeedback and brain activation patterns, the methods and results of which have been previously reported [9].

2.3. Data analysis

Data analysis was completed using standard pre-surgical functional mapping procedures. Temporal signal space separation and head position estimation was completed on all MEG data (Maxfilter, Elekta AB, Stockholm, SE) [10]. Datasets were excluded from further analysis if rotation or translation exceeded 3 degrees or 5 mm, respectively. Data was then down sampled to 250 Hz and a low-pass filter of 70 Hz was applied to attenuate any high-frequency noise. Lastly, an additional artifact removal was done using independent component analysis to remove artifacts, including components that were highly correlated with the electrooculogram time course [11]. The filtered data was then epoched into 600 ms sections (100 ms pre-stimulus to 500 ms post-stimulus) using the event markers for stimulation onset. The resulting 160 epochs were binned according to side ($N = 80$ for the left and right hemisphere, respectively) and averaged. Baseline correction was applied using a pre-stimulus window of −50 to −25 ms. The somatosensory evoked field (SEF) pattern was then manually selected as the field topography at the