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Retrospective comparison of motor and somatosensory MEG mapping—Considerations for better clinical applications

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ABSTRACT

While magnetoencephalography (MEG) has proven to be a valuable and reliable tool for presurgical functional mapping of eloquent cortices for at least two decades, widespread use of this technique by clinicians has remained elusive. This modest application may be attributable, at least in part, to misunderstandings regarding the success rate of such mapping procedures, as well as the primary sources contributing to mapping failures. To address this, we conducted a retrospective comparison of sensorimotor functional mapping success rates in 141 patients with epilepsy and 75 tumor patients from the Center for MEG in Omaha, NE. Neurosurgical candidates either completed motor mapping (i.e., finger tapping paradigm), somatosensory mapping (i.e., peripheral stimulation paradigm), or both motor and somatosensory protocols during MEG. All MEG data underwent subsequent time-domain averaging and source localization of left and right primary motor (M1) and somatosensory (S1) cortices was conducted using a single equivalent dipole model. Successful mapping was determined based on dipole goodness of fit metrics ~ 95%, as well as an accurate and conceivable spatial correspondence to precentral and postcentral gyri for M1 and S1, respectively. Our results suggest that mapping M1 in epilepsy and tumor patients was on average 94.5% successful, when patients only completed motor mapping protocols. In contrast, mapping S1 was successful 45–100% of the time in these patient groups when they only completed somatosensory mapping paradigms. Importantly, Z-tests for independent proportions revealed that the percentage of successful S1 mappings significantly increased to ~ 94% in epilepsy patients who completed both motor/somatosensory mapping protocols during MEG. Together, these data suggest that ordering more comprehensive mapping procedures (e.g., *both* motor and somatosensory protocols for a collective sensorimotor network) may substantially increase the accuracy of presurgical functional mapping by providing more extensive data from which to base interpretations. Moreover, clinicians and magnetoencephalographers should be considerate of the major contributors to mapping failures (i.e., low SNR, excessive motion and magnetic artifacts) in order to further increase the percentage of cases achieving successful mapping of eloquent cortices.

1. Introduction

Despite being a well-known tool for functional brain mapping, the use of magnetoencephalography (MEG) by clinicians for the presurgical delineation of eloquent cortices including motor, somatosensory, visual, auditory and language areas, has been modest. This limited clinical use of MEG protocols may be attributable, at least in part, to a general lack of knowledge regarding the practical recommendations, including ordering and interpreting MEG clinical mapping results, as well as potential sources of error that should be considered in order to improve the success rate of mapping procedures. In fact, recent surveys of MEG centers and associated clinics note that more evidence regarding the clinical efficacy of MEG, as well as more informative MEG reporting, training and adherence to recommended guidelines may augment the broader application of MEG in the future (Bagić, 2011; Bagić and Burgess, 2020a, 2020b). These issues were above and beyond those of technical limitations like the proximity of clinics to MEG centers, insurance issues or lack of complex surgical candidates. Thus, it is imperative to improve communication amongst clinicians, neurosurgeons, patients, and magnetoencephalographers alike regarding the

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utility and empirical success of MEG as a leading tool for presurgical mapping.

Of the functional mapping protocols ordered prior to surgical resection, somatosensory and motor mapping procedures are collectively, the most common for a patient to complete (Bagić et al., 2017; Bagić and Burgess, 2020a). This is especially true when the lesion or tumor is adjacent to the sensorimotor strip, or when the epileptogenic zone(s) are suspected to reside near sensorimotor cortex in non-lesional cases. Nevertheless, the ultimate goal of sensorimotor functional mapping is to *(1)* delineate anatomical landmarks including the central sulcus, *(2)* identify the precise location of pre- and postcentral gyri related to motor and somatosensory functionality, respectively, and *(3)* confirm the anatomical location (e.g., anterior-to-posterior orientation) of each in relation to one another to not only aid the success of surgical resections, but also to assess potential functional risks that may evolve post-resection (Bowyer et al., 2020; De Tiège et al., 2020). To achieve this, most magnetoencephalographers and/or clinicians employ source localization of motor and somatosensory evoked fields (MEF and SEF, respectively) using equivalent current dipole (ECD) models resulting from trial-averaged movements or peripheral (i.e., mechanical or electrical) stimulation data for motor and somatosensory functionality of the targeted limb, respectively (Bowyer et al., 2020). While these approaches are known to provide some of the most precise and reliable results among presurgical, noninvasive functional mapping procedures, as evidenced by good spatial correspondence with gold standard intraoperative direct current stimulation (Ishibashi et al., 2001; Morioka et al., 1995; Oishi et al., 2003; Pang et al., 2008; Schiffbauer et al., 2002; Solomon et al., 2015), there remains widespread variability in the amount of successful sensorimotor mapping that is achieved across study cohorts.

For example, previous studies suggest that the success rate of precisely localizing motor and somatosensory upper limb functionality using MEG ranges anywhere from 41 to 100%, with even lower success rates reported for mapping lower limb or ipsilateral hemispheric functionality (~14–36%) (Kober et al., 2001; Lin et al., 2006; Oishi et al., 2003; Pang et al., 2008; Schiffbauer et al., 2002; Willemse et al., 2016). This varied success in motor and somatosensory localization may be attributable, at least in part, to the inconsistent ordering of both motor *and* somatosensory mapping paradigms for correspondent source localization, which aids in interpretation of the final results. Essentially, due to the relative ease of passive somatosensory stimulation protocols compared to the even slightly more demanding movement-based paradigms used for motor mapping procedures (e.g., finger tapping), concomitant with the established reliability of localizing SEF (Ishibashi et al., 2001; Okada et al., 1984; Solomon et al., 2015), clinicians may order only one mapping procedure to localize *both* motor and somatosensory functionality. This is a surprising adaptation, as one of the primary objectives of presurgical sensorimotor mapping requires the precise demarcation of the anatomical relationships between pre- and postcentral gyri, which could be substantially improved upon completion of more comprehensive mapping procedures (i.e., completion of motor *and* somatosensory mapping protocols during MEG).

To this end, we aimed to retrospectively compare sensorimotor mapping success rates in a large sample of neurosurgical candidates (141 with epilepsy, 75 with tumors) who completed only single presurgical mapping protocols (i.e., only a motor or somatosensory protocol during MEG) and those who completed a more comprehensive sensorimotor procedure (i.e., both motor/somatosensory protocols during MEG) during presurgical planning. We hypothesized that the successful anatomical localization of primary motor (i.e., precentral gyri) and somatosensory (i.e., postcentral gryi) cortices would be significantly improved (i.e., greater proportion of study cohort identified as successful mapping) in those who completed both motor and somatosensory MEG mapping procedures as opposed to single protocols alone. Moreover, we summarize the most common sources of mapping failures observed in our cohort, which may support greater mapping successes of eloquent cortices using MEG in the future.

2. Materials and methods

2.1. Participant demographics

We conducted a retrospective comparison of 141 patients with epilepsy and 75 tumor patients who underwent presurgical functional mapping of eloquent cortices at the Center for MEG at the University of Nebraska Medical Center (UNMC; Omaha, NE). Of the 141 patients with epilepsy, 135 (50 female, M = 30.6 years old, range: 8–65 years old, 56 right handed) underwent either motor, somatosensory or both motor/somatosensory MEG upper limb mapping protocols and were included in the final analyses (Fig. 1). Likewise, 59 of the 75 tumor patients (10 female, M = 42.6 years old, range: 6–74 years old, 23 right handed) who completed either motor, somatosensory or both motor/somatosensory MEG upper limb mapping procedures were included in the final analyses (Fig. 1). Of note, patients were excluded from motor and/or somatosensory mapping procedures based on the referring clinician's orders. The exclusion of one or more modalities was most commonly attributable to the location of tumor(s), lesion(s), and/or the suspected epileptogenic zone(s) being outside of the sensorimotor strip (i.e., pre- or postcentral gryi). In addition, the focus on upper limb functionality in the current study was based on the referring clinician's orders, which more commonly requested upper limb testing compared to the testing of other extremities. The study protocol was approved by the IRB of UNMC.

2.2. Motor and somatosensory mapping paradigms

Patients were seated in a nonmagnetic chair with their head positioned within the helmet-shaped array. To localize left and right primary motor cortices (M1), participants completed a quasi-paced finger tapping paradigm where participants were asked to perform a single flexion–extension of the index finger each time a red dot reached the target interval denoted in blue, which was located near the 12o'clock position. This dot completed a full rotation around the clock-like design (without tick marks or numbers) every 5.5 s, and was meant to serve as a pacing mechanism (Heinrichs-Graham et al., 2014, 2017; Spooner et al., 2021b; Wilson et al., 2010; Wilson et al., 2011; Wilson et al., 2011; Wilson et al., 2013, 2014). To detect movement onset with high temporal precision, a custom pad with a laser-based circuit that was occluded until movement was initiated was used. Patients completed ~ 90 trials using their left and right index fingers, separately. The total time to complete the experiment with both limbs was approximately 16 min.

For localization of primary somatosensory cortices (S1), patients received electrical stimulation of the median nerve using external cutaneous stimulators connected to a Digitimer DS7A constant-current stimulator system (Digitimer Ltd, Garden City, UK). For each patient, we collected 240 pulses with an inter-stimulus interval that varied from 0.45 to 0.60 s. Each pulse consisted of a 0.2 ms constant-current square wave that was set to 10% above the individual's motor threshold. Patients received passive stimulation (i.e., ~240 pulses) on their left and right median nerve, separately. The total time to complete the experiment with both limbs was approximately two minutes.

2.3. MEG data acquisition

All recordings were performed in a one-layer magnetically shielded room with active shielding engaged for environmental noise compensation. With an acquisition bandwidth of 0.1–330 Hz, neuromagnetic responses were sampled continuously at 1 kHz using an Elekta/MEGIN MEG system (MEGIN, Helsinki, Finland) with 306 magnetic sensors, including 204 planar gradiometers and 102 magnetometers. Throughout data acquisition, patients were monitored using a real-time audio–video feed from inside the magnetically shielded room. MEG data were subjected to noise reduction using the signal-space separation method with

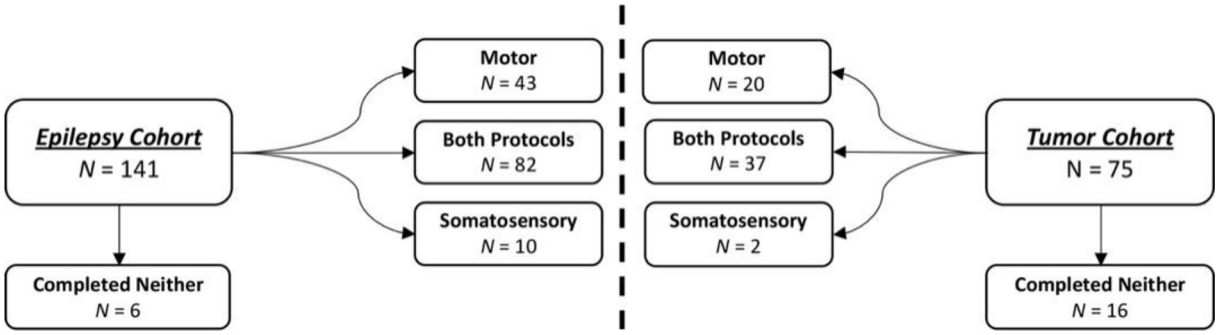

Fig. 1. Flow Diagram. A total of 141 patients with epilepsy and 75 tumor patients completed presurgical mapping at the Center for MEG at the University of Nebraska Medical Center. A retrospective comparison of sensorimotor cortical mapping was conducted on those who completed either motor (N = 43 epilepsy, 20 tumor), somatosensory (N = 10 epilepsy, 2 tumor) or both motor/somatosensory (N = 82 epilepsy, 37 tumor) mapping protocols. Note that the two groups (epilepsy and tumor) were examined independently in all analyses.

a temporal extension (tSSS; (Taulu and Simola, 2006)).

2.4. Structural MRI processing and MEG coregistration

Prior to MEG measurement, four coils were attached to the participant's head and the locations of these coils, together with three fiducial points and scalp surface, were digitized with a 3D digitizer (Fastrak 3SF0002, Polhemus Navigator Sciences, Colchester, VT, USA). Once the patient was positioned for MEG recording, an electric current with a unique frequency label (e.g., 322 Hz) was fed to each of the coils, which induced a measurable magnetic field that allows each coil to be localized in reference to the sensors throughout the recording sessions. Since the coil locations were also known in head coordinates, all MEG measurements could be transformed into a common coordinate system, which allowed each patient's MEG data to be coregistered to their T1-weighted structural magnetic resonance images (MRI) prior to source space analyses. All MRI data were acquired with a Philips Achieva 3 T X-series scanner using an 8-channel head coil (TR: 8.09 ms; TE: 3.7 ms; field of view: 240 mm; slice thickness: 1 mm; no gap; in-plane resolution: 1.0 × 1.0 mm). All MRI data were aligned parallel to the anterior and posterior commissures.

2.5. MEG Preprocessing, source localization and determination of successful mapping

Cardiac and ocular artifacts were removed from the data using signal-space projection (SSP;(Uusitalo and Ilmoniemi, 1997)). Epochs were of 2.5 s duration, with 0.0 s defined as movement onset for finger tapping paradigms and the baseline being the −1.0 to −0.5 s time window. For somatosensory paradigms, epochs were of 0.3 s duration, with 0.0 s defined as stimulation onset and the baseline being the −0.05 to 0.0 s window. Epochs containing artifacts were excluded using a fixed threshold method (i.e., based on artifactual neural amplitude values), supplemented with visual inspection (Christopher-Hayes et al., 2021; Spooner et al., 2021a; Wiesman et al., 2021). Artifact-free epochs were time-domain averaged with respect to movement or stimulation onset. For each patient, the temporal window of signal maxima *peri*-movement (from −100 to 150 ms window) or post-stimulation (~20–80 ms window) onset was defined uniquely for each extremity and patient and modeled using a single-moving, equivalent current dipole (ECD). Determination of successful M1 and S1 functional mapping included resulting ECD solutions that met the 95% goodness of fit (GOF) metric (i.e., solutions that account for at least 95% of the variance in the filtered MEG data). In addition, successful mapping designations required a conceivable spatial localization to precentral and postcentral gryi for motor and somatosensory mapping procedures, respectively, as well as their relation to the central sulcus based on well-established anatomical MRI landmarks (i.e., presence of hand knob feature of the precentral gyri, anterior bank of central sulcus for motor, posterior bank for somatosensory (Yousry et al., 1997); for exemplary mapping in patients performing single and comprehensive mapping procedures, see Fig. 2). In addition, patients who underwent both motor/somatosensory mapping required a conceivable anterior-to-posterior anatomical orientation of motor-to-somatosensory ECD localizations to be considered a successful mapping. More information regarding our standard MEG source localization procedures can be found in our previous publications (Ellis et al., 2020; Kurz and Wilson, 2011; Wilson et al., 2007, 2005a, 2005b). The proportion of successful mapping of left and right M1 and S1 is reported separately for epilepsy and tumor patients. In order to evaluate potential differences in mapping accuracy based on whether patients completed single (e.g., motor only protocol) or comprehensive mapping procedures (i.e., both motor/somatosensory protocols), Z-tests for independent proportions were conducted. Finally, observed contributors to mapping failures are reported separately for the patient groups.

3. Results

3.1. Motor mapping success rates for epilepsy and tumor patients

Our retrospective comparison of M1 mapping success rates demonstrated relatively high success in mapping the left and right M1 based on ECD solutions in patients, with an average success rate of 92.6% regardless of mapping protocol (i.e., single or comprehensive), hemisphere (i.e., left or right), or patient population (i.e., epilepsy or tumor). For patients with epilepsy, 43 patients completed only motor mapping paradigms (i.e., finger tapping), while 82 patients completed both motor and somatosensory mapping protocols (i.e., finger tapping and peripheral stimulation). Our results showed that mapping the left and right M1 was 95.3% and 93.0% successful, respectively, for patients who only completed the motor mapping protocol during MEG (Fig. 3). Interestingly, 87.8% and 85.4% of patients had successful ECD mapping of left and right M1, respectively (Fig. 3), when undergoing *both* motor/somatosensory mapping protocols, albeit this difference in mapping success was not significantly reduced compared to those completing only the motor paradigm (left M1 motor only vs. both: $Z = 1.35$, $p = .177$, 95% CI [-0.03, 0.18]; right M1 motor only vs. both: $Z = 1.26$, $p = .209$, 95% CI [-0.04, 0.20]).

For tumor patients, 20 patients completed only motor mapping protocols during MEG, while 37 patients completed both motor and somatosensory paradigms. Our results showed that mapping the left and right M1 was 95% successful for patients who only completed the motor mapping protocol (Fig. 4). Additionally, 97.3% and 91.9% of tumor patients revealed successful mapping of left and right M1, respectively, when both motor/somatosensory protocols were performed. Importantly, this change in mapping success did not significantly differ from those who only completed the motor mapping paradigm (left M1 motor

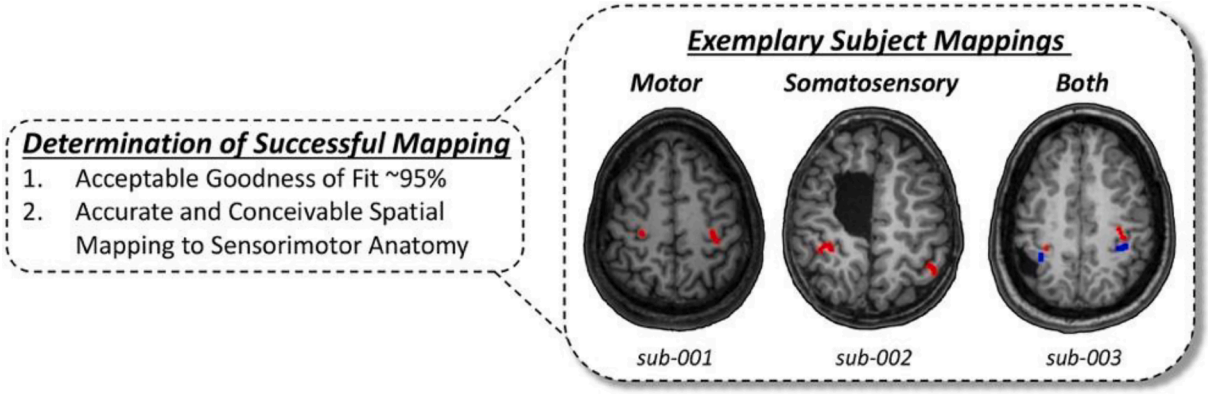

Fig. 2. Successful Mapping Protocol and Exemplary Subjects. Determination of successful mapping procedures for motor and somatosensory cortices required dipole modeling goodness of fit metrics equal to or greater than 95% and an accurate and plausible spatial mapping to the sensorimotor cortices. Successful single moving dipole solutions for three representative subjects (see right panel) who completed motor mapping protocols only (left), somatosensory mapping protocols only (middle), or both protocols (right).

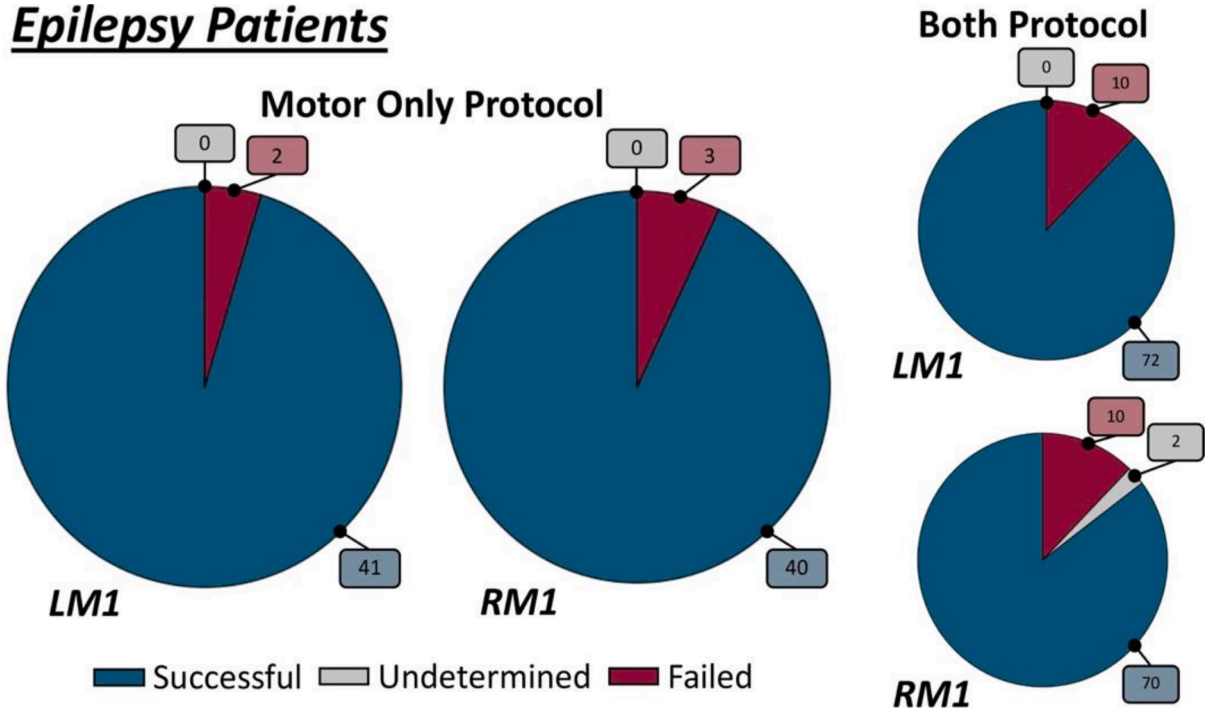

Fig. 3. Motor Cortex Mapping Success Rates in Epilepsy Patients. Pie charts showing the number of epilepsy patients who had successful mapping of left and right primary motor cortices (LM1 and RM1, respectively) through completion of motor mapping protocols only (left panel), as well as both motor/somatosensory mapping protocols (right panel). $N_{motor} = 43$, $N_{both} = 82$.

only vs. both: $Z = -0.39$, $p = .695$, 95% CI [-0.12, 0.08]; right M1 motor only vs. both: $Z = 0.43$, $p = .668$, 95% CI [-0.11, 0.17]).

3.2. Somatosensory mapping success rates for epilepsy and tumor patients

Retrospective comparisons of S1 functional mapping based on ECD solutions revealed an average success rate of 83.7%, irrespective of mapping protocol, hemisphere, and patient population. For patients with epilepsy, 10 patients completed only somatosensory mapping paradigms (i.e., peripheral stimulation), while 82 patients completed both motor and somatosensory mapping protocols (i.e., finger tapping and peripheral stimulation). Interestingly, our results showed relatively low success in mapping the left and right S1 for those patients who only completed the somatosensory mapping paradigm during MEG (50% and 40% successful for left and right S1, respectively; Fig. 5). However, there was a significant increase in mapping success (i.e., 93.9% success rate) for patients who completed both motor and somatosensory mapping paradigms during MEG (left S1 somatosensory only vs. both: $Z = -4.21$, $p < .001$, 95% CI [-0.64, −0.24]; right S1 somatosensory only vs. both: $Z = -4.96$, $p < .001$, 95% CI [-0.75, −0.33]).

For tumor patients, only 2 patients completed the somatosensory-only protocol during MEG, which resulted in successful mapping of the left and right S1 in both patients (Fig. 6). Of the 37 patients who completed both motor and somatosensory mapping procedures, 97.3% and 94.6% revealed successful mapping of the left and right S1, respectively, and importantly, S1 mapping accuracy did not significantly differ from those who only completed the peripheral stimulation protocol (left S1 somatosensory only vs. both: $Z = 0.24$, $p = .814$, 95% CI [-0.20, 0.25]; right S1 somatosensory only vs. both: $Z = 0.34$, $p = .736$, 95% CI [-0.26, 0.37]).

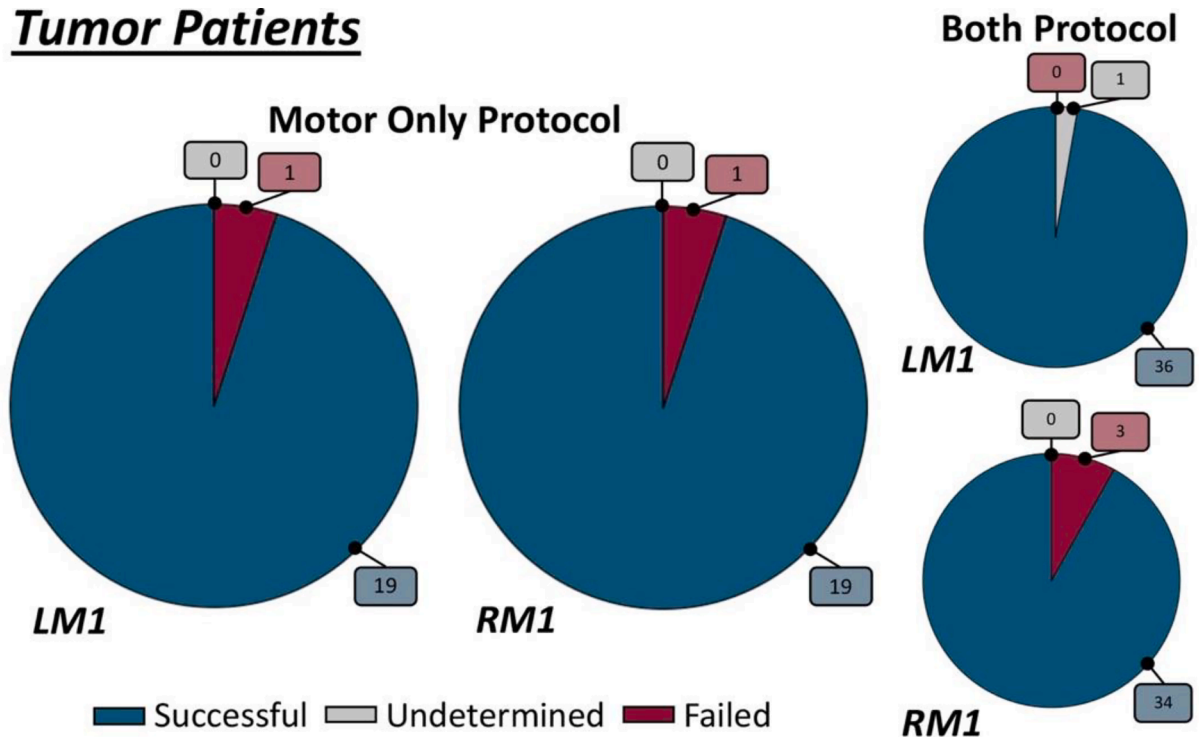

Fig. 4. Motor Cortex Mapping Success Rates in Tumor Patients. Pie charts showing the number of tumor patients who had successful mapping of left and right primary motor cortices (LM1 and RM1, respectively) through completion of motor mapping protocols only (left panel), as well as both motor/somatosensory mapping protocols (right panel). $N_{motor} = 20$, $N_{both} = 37$.

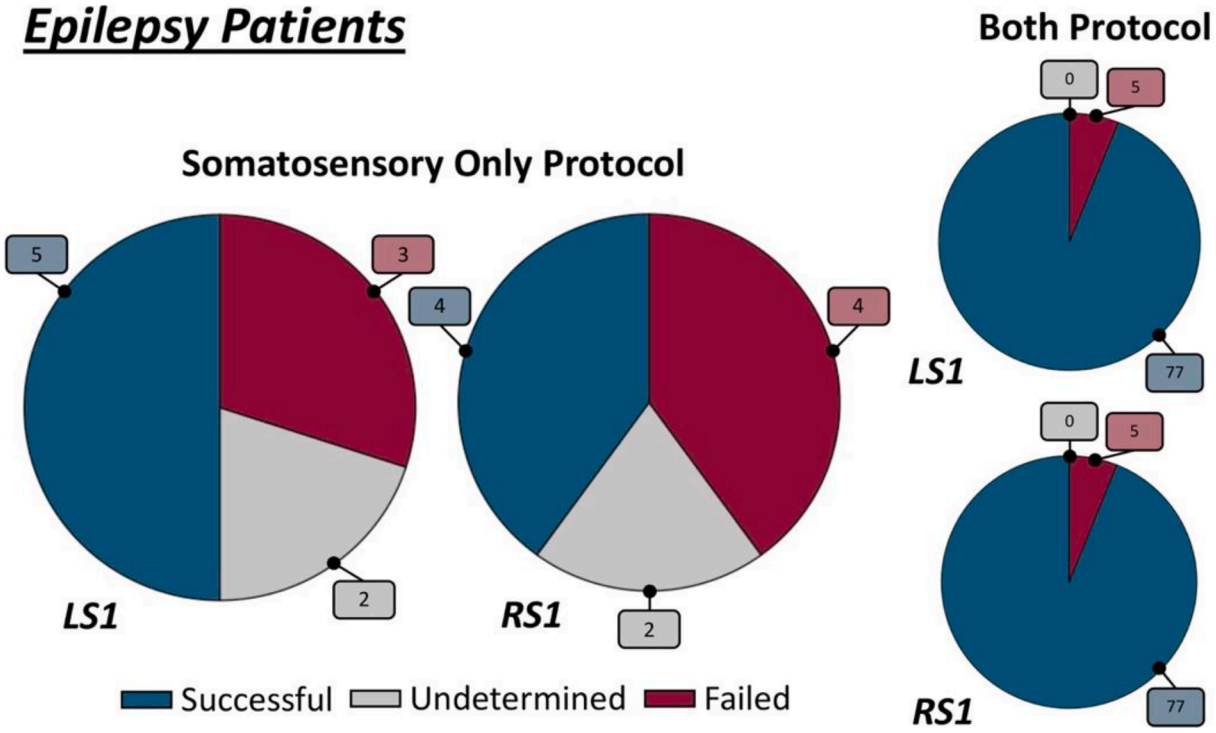

Fig. 5. Somatosensory Cortex Mapping Success Rates in Epilepsy Patients. Pie charts showing the number of epilepsy patients who had successful mapping of left and right primary somatosensory cortices (LS1 and RS1, respectively) through completion of somatosensory mapping protocols only (left panel), as well as both motor/somatosensory mapping protocols (right panel). $N_{somatosensory} = 10$, $N_{both} = 82$.

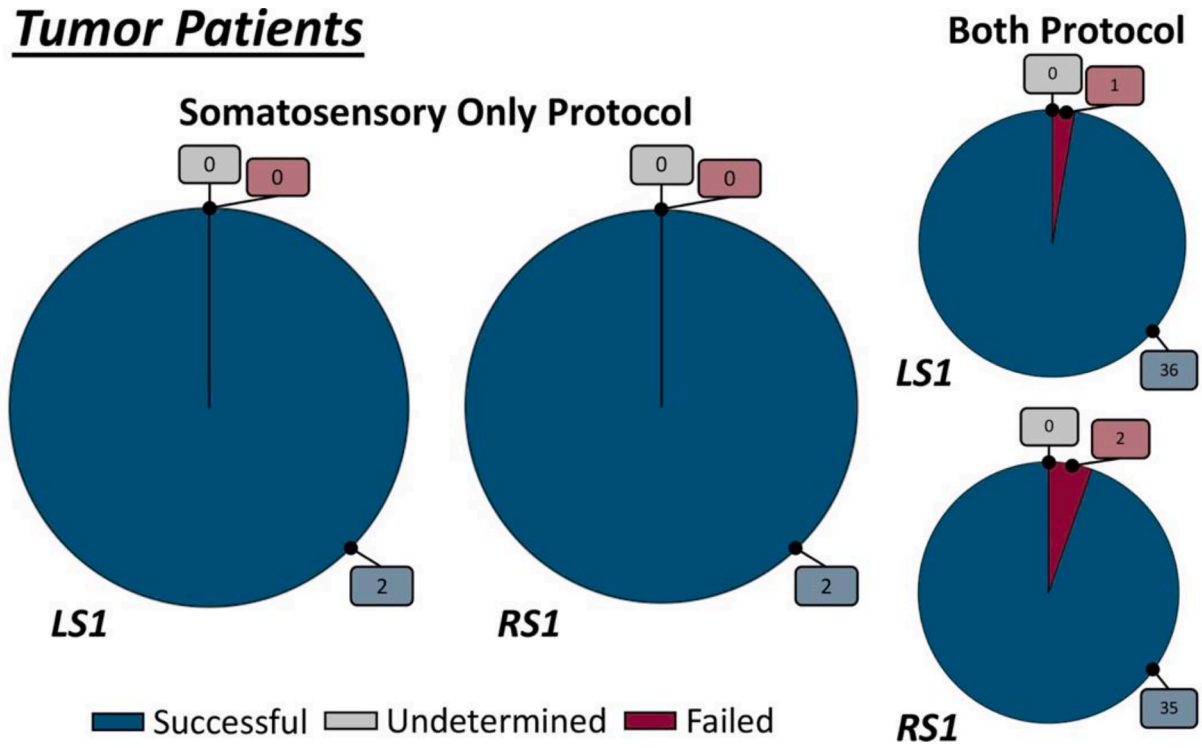

Fig. 6. Somatosensory Cortex Mapping Success Rates in Tumor Patients. Pie charts showing the number of tumor patients who had successful mapping of left and right primary somatosensory cortices (LS1 and RS1, respectively) through completion of somatosensory mapping protocols only (left panel), as well as both motor/somatosensory mapping protocols (right panel). $N_{somatosensory} = 2$, $N_{both} = 37$.

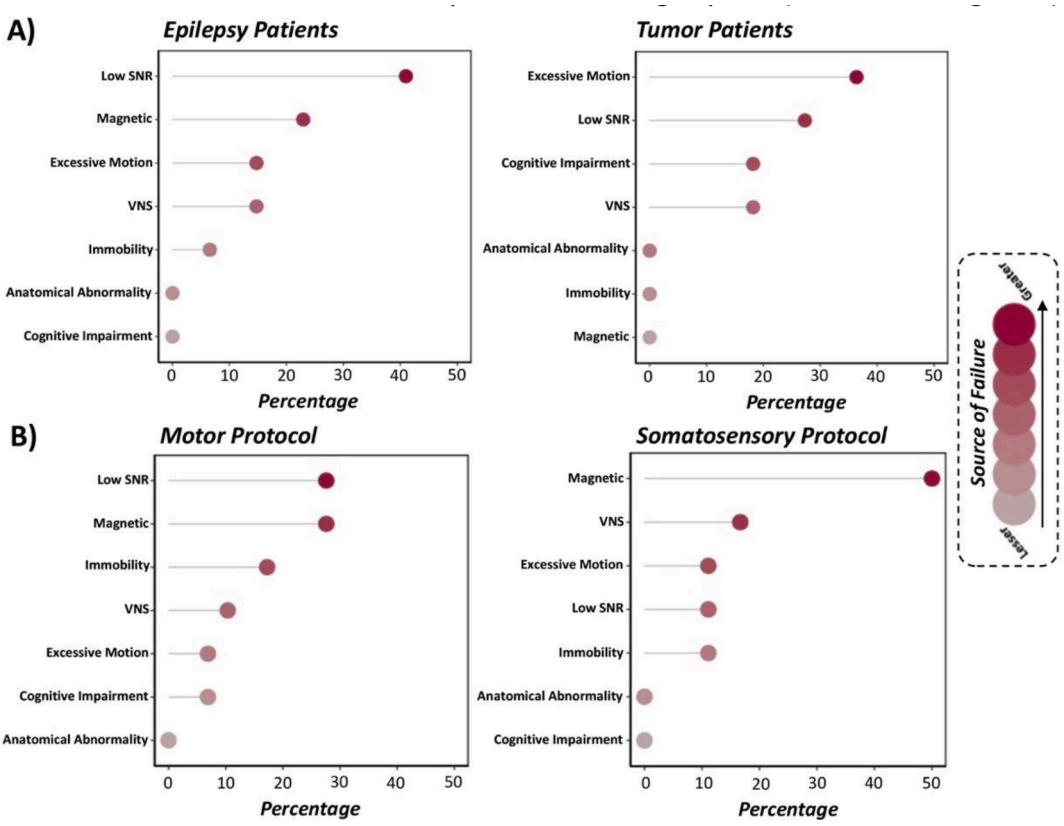

Fig. 7. Sources of Unsuccessful Functional Mapping. (A) Lollipop charts denoting the sources of mapping failures as a function of patient group (i.e., epilepsy ($N_{total} = 135$) and tumor patients ($N_{total} = 59$)) and (B) as a function of mapping modality (i.e., motor only/both, somatosensory only/both). Sources of mapping failures included low SNR, excessive motion, magnetic implants (e.g., dental work), presence of a vagal nerve stimulator (VNS), peripheral immobility, anatomical atrophy/abnormality and cognitive impairment.

3.3. Sources of error contributing to mapping failures in neurosurgical candidates

Finally, we aimed to evaluate the largest contributors to sensorimotor mapping failures in patients with epilepsy (N = 135) and tumors (N = 59), regardless of mapping protocol (i.e., motor only, somatosensory only, both motor/somatosensory protocol). Investigator-identified sources of mapping failures included low signal to noise ratio (SNR), excessive motion artifacts from the patient, ferromagnetic artifacts (e.g., dental work), presence of a vagal nerve stimulator (VNS), peripheral immobility, anatomical atrophy/abnormality and cognitive impairment. Of the 135 patients with epilepsy who received sensorimotor presurgical mapping, 39 patients (28.9% of the total epilepsy cohort) had undetermined or failed sensorimotor mappings as evidenced by GOF metrics < 95% and/or inconceivable spatial mapping. The largest sources of mapping failures for epilepsy patients (N = 39) were low SNR (41.0%), ferromagnetic implants (23.0%), presence of a VNS (14.8%), excessive motion artifacts (14.8%), and peripheral immobility (6.6%; Fig. 7). In regard to tumor patients, 8 patients (13.6% of the total tumor cohort) had undetermined or failed sensorimotor mappings. The largest contributors to mapping failures in these patients (N = 8) were excessive patient motion (36.4%), low SNR (27.3%), the presence of a VNS (18.2%), and cognitive impairment (18.2%; Fig. 7). For completeness, we also striated mapping failures as a function of mapping modality to provide a more comprehensive overview of the sources of mapping failures. These data suggest that the largest sources of *motor* mapping failures (N = 29) included low SNR (27.6%), magnetic implants (27.6%), and immobility (17.2%), albeit the presence of a VNS (10.3%), excessive motion (6.9%) and cognitive impairment (6.9%) also contributed to failed motor mappings. Likewise, for *somatosensory* mappings (N = 18), the largest sources of failures were ferromagnetic implants (50%) and the presence of a VNS (16.7%), while excessive motion, low SNR and immobility contributed slightly less (~11% each; Fig. 7).

4. Discussion

The current study aimed to retrospectively compare the success of presurgical sensorimotor mapping using single (e.g., motor only) and comprehensive (i.e., both motor/somatosensory) mapping procedures during MEG in a relatively large sample of epilepsy and tumor patients. Specifically, we found that mapping M1 (i.e., precentral gyri) yielded relatively high success rates (~93%) regardless of mapping protocol (i.e., single or comprehensive), hemisphere (i.e., left or right), and patient population (i.e., epilepsy or tumor patients). In contrast, mapping primary somatosensory cortices (i.e., postcentral gyri) was much less successful (~45%) for epilepsy patients who only completed somatosensory mapping protocols during MEG. However, this success was substantially improved upon completion of comprehensive mapping procedures (~94%). Finally, we observed that the majority of mapping failures largely resulted from low SNR, excessive motion and ferromagnetic artifacts impeding effective source localization, as well as peripheral immobility or cognitive impairment limiting task completion. Importantly, our results provide insight regarding the methodological considerations that may substantially increase sensorimotor mapping accuracy in the future. The implications of these novel findings are discussed below.

Our most important finding was likely the substantial increase in S1 mapping success observed in epilepsy patients who completed comprehensive mapping procedures (i.e., both motor/somatosensory) during MEG compared to those who completed peripheral stimulation protocols alone. This finding was somewhat surprising, as MEG-based somatosensory evoked field (SEF) localization are revered as one of the most robust and reliable signals observed in the literature (Ishibashi et al., 2001; McCusker et al., 2021; Okada et al., 1984; Solomon et al., 2015), and thus, completion of these protocols were expected to be quite effective on their own. Nevertheless, our results suggest that ordering more comprehensive mapping procedures to precisely localize *both* motor and somatosensory cortices may improve mapping accuracy of S1 alone. Thus, accurate functional localization may be easier to achieve when multiple perspectives are provided to the clinician and/or magnetoencephalographer, therefore providing the investigator with more confidence in the respective mappings of motor *and* somatosensory cortices, especially within the context of their anatomical orientation to one another. Interestingly, we did not observe a change in S1 mapping success rates as a function of mapping procedure in tumor patients, albeit these results should be interpreted with caution due to the small sample size of those who only completed somatosensory mapping paradigms in the current study. Finally, in contrast to somatosensory localization success, we did not observe a significant change in mapping success rates of the left and right M1 as a function of mapping procedure, although M1 mapping success was the highest across all neurosurgical candidates (~93%), and importantly, was not significantly affected by completion of single versus comprehensive mapping procedures.

Finally, our study is the first to concurrently report various contributions to the mapping failures observed in our cohort. Across all patients, the most common sources of mapping failures included low SNR, excessive motion artifacts and the presence of ferromagnetic artifacts (e.g., dental work), including a VNS. In addition, we observed instances where peripheral immobility and cognitive impairment also contributed to mapping failures in epilepsy and tumor patients, respectively. Taken together, we propose that future applications of presurgical MEG mapping would benefit from more standardized methodological parameters such as increased trial counts, to counteract trial rejection due to excessive motion or magnetic-related artifacts that will inevitably result in low SNR (Baillet, 2017; Hämäläinen et al., 1993; Wilson et al., 2016). Similarly, it will be imperative for paradigms to incorporate sufficient inter-stimulus intervals between trials to facilitate the effective return of neural responses to a noise-free baseline in order to enhance the SNR for subsequent trial averaging and source localization analyses (Laohathai et al., 2021; Wilson et al., 2016). Finally, it is not surprising that peripheral immobility and cognitive impairment contributed to mapping inaccuracies and importantly, suggests that some proportion of mapping failures result from the patient's inability to complete the task.

While the finger flexion–extension paradigm used in the current study has been previously vetted in both healthy and clinical populations in our laboratory (Heinrichs-Graham et al., 2014, 2017; Spooner et al., 2021b; Wilson et al., 2010; Wilson et al., 2011; Wilson et al., 2011; Wilson et al., 2013, 2014), the task still requires the active initiation and completion of a movement with the index finger. Moreover, it also requires some attentional component to the pacing mechanism (i.e., clock-like design), which recent evidence suggests that deficits in attention may modulate the neural and behavioral mechanisms serving motor control (Gaetz et al., 2013; Grent-'t-Jong et al., 2013; Heinrichs-Graham et al., 2018; Spooner et al., 2020c; Wiesman et al., 2020). Thus, the application of passive and/or simultaneous sensorimotor paradigms whereby patients are not required to actively engage in or attend to a movement could effectively ameliorate this contribution to mapping failures. For example, Castillo and colleagues evaluated the validity of a simultaneous motor/somatosensory paradigm and showed intraoperatively-verified robust SEF and MEF components during sequential mechanical stimulation and flexion–extension movements of the hand, respectively, albeit this paradigm still required active movement engagement by the participants (Castillo et al., 2004). To rectify this limitation, we propose that future studies examining simultaneous motor/somatosensory mapping should evaluate the utility of suprathreshold somatosensory stimulation paradigms, whereby electrical stimulation of the median or tibial nerve is applied ~ 10% above the motor threshold to elicit a subtle movement of the respective digit. Importantly, this paradigm has been shown to elicit robust somatosensory evoked and high-frequency oscillatory neural responses immediately following electrical stimulation in healthy and clinical populations

(e.g., aging, cerebral palsy, HIV (Cheng et al., 2016; Kurz et al., 2018; Lenz et al., 2012; Spooner et al., 2021; Spooner et al., 2020a, 2020b, 2019, 2018; Wiesman et al., 2017)), with a subsequent recruitment of movement-related oscillations including event-related desynchronizations and resynchronizations in the beta range (i.e., 15–30 Hz) during the passive movement (Cheng et al., 2017). Furthermore, this paradigm has demonstrated good-to-excellent reliability in its source reconstructed neural responses (i.e., intraclass correlation) across subjects upon a 36-month longitudinal follow-up (McCusker et al., 2021). Although median or tibial nerve electrical stimulation paradigms exceeding the individual's motor threshold have been the proposed clinical standard for over a decade by the American Clinical Magnetoencephalography Society (ACMEGS; (Burgess et al., 2011)), the use of this approach to simultaneously map *both* somatosensory *and* motor cortices for presurgical planning has yet to be fully realized. Nevertheless, these data demonstrate the promise of this paradigm as a valuable candidate for simultaneous and passive sensorimotor functional MEG mapping in the future.

5. Conclusions

To conclude, this study was the first to establish the contribution of comprehensive mapping procedures for the successful localization of sensorimotor cortices in a large cohort of epilepsy and tumor patients. Specifically, we observed a substantial improvement in upper limb mapping success rates for S1 cortices when patients completed a comprehensive mapping protocol (i.e., both motor *and* somatosensory procedures) compared to those who only completed a single mapping procedure during MEG (i.e., only peripheral stimulation). Interestingly, M1 mapping did not differ as a function of mapping procedure. In addition, we report that the most common sources of mapping failures observed in the current cohort included low SNR, excessive motion artifacts and ferromagnetic implants, although peripheral immobility and cognitive impairment also contributed to failed sensorimotor mappings in our patients. Together, these data suggest that the application of more comprehensive mapping procedures may significantly increase the rate of successful sensorimotor functional mappings in neurosurgical candidates. However, there are several additional acquisition procedures that should be considered by magnetoencephalographers and/or clinicians to improve mapping accuracies, including the standardization of methodological parameters (e.g., increased trial counts or inter-stimulus intervals to combat low SNR due to extensive artifacts and/or noise (Baillet, 2017; Hämäläinen et al., 1993; Laohathai et al., 2021; Wilson et al., 2016)), as well as the implementation of passive, simultaneous motor/somatosensory mapping paradigms (e.g., using suprathreshold peripheral stimulation (Spooner et al., 2019, 2020a; Burgess et al., 2011)) to eliminate potential patient-related errors in task completion. Finally, future studies will undoubtably benefit from standardizing the methods for defining mapping success including acceptable GOF metrics, as well as ECD spatial specificity and reproducibility (Laohathai et al., 2021), especially in the presence of anatomical abnormalities which may substantially shift this criterion in some cases. Oftentimes, the perceived success of MEG mapping procedures drives surgical planning decisions such as the need for additional preoperative mapping (e.g., with functional MRI (fMRI) and/or intraoperative procedures, and thus the capacity to derive more definitive conclusions would have a major clinical impact. Moreover, comparisons of the MEG mapping techniques outlined herein to gold standards for functional mapping (e.g., invasive electrocortical stimulation) will undoubtably expand our understanding of the utility of these noninvasive metrics for pre- and post-central gyri sensorimotor mapping in the future. In addition, the number of presurgical mapping successes may be substantially increased by expanding upon the sole use of ECD-related approaches to the analysis of additional neurophysiological metrics that may prove informative for sensorimotor mapping accuracy (e.g., movement or stimulation-induced oscillatory dynamics (De Tiège et al., 2020)). This is especially pertinent given the recent evidence implicating sensorimotor oscillatory dynamics (e.g., 15–30 Hz beta and greater than 30 Hz gamma activity) as more sensitive markers of external as well as participant-related factors (e.g., paradigm variations, age, disease status) compared to sensorimotor time-domain responses alone (Rachel K Spooner et al., 2021b; Spooner et al., 2021; Spooner et al., 2020a, 2019). *En masse*, it will be of utmost importance for future studies to evaluate such standardization procedures to facilitate comparison of the results and implications presented herein to other clinical sites and neurosurgical candidates assessed across the world.

CRediT authorship contribution statement

Rachel K. Spooner: Conceptualization, Formal analysis, Funding acquisition, Investigation, Writing – original draft, Writing – review & editing. **Deepak Madhavan:** Data curation, Methodology, Investigation. **Michele R. Aizenberg:** Data curation, Methodology, Investigation. **Tony W. Wilson:** Conceptualization, Data curation, Methodology, Funding acquisition, Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors have no financial, commercial or institutional conflicts of interest to declare.

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