Biomagnetic signals recorded during transcranial magnetic stimulation (TMS)-evoked peripheral muscular activity

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Transcranial magnetic stimulation (TMS) has widespread clinical applications from diagnosis to treatment approaches. We combined TMS with non-contact magnetic detection of TMS-evoked muscle activity in peripheral limbs to explore a new diagnostic modality that enhances the utility of TMS as a clinical tool by leveraging technological advances in magnetometry. We recorded measurements inside of a hospital using an array of optically pumped magnetometers (OPMs) inside a portable shield that encompasses only the forearm and hand of the subject. We present magnetomyograms (MMGs) of TMS-evoked movement in a human hand, together with a simultaneous surface electromyograph (EMG) and electroencephalograph (EEG) data. The biomagnetic signals recorded in the MMG provides detailed spatial and temporal information that is complementary to that of the electric signal channels. Moreover, we identify features in the magnetic recording beyond that of the EMG, at time points which we further analyze in the EEG. This system demonstrates the value of biomagnetic signals in TMS-based clinical approaches and widens its availability and practical potential.

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arXiv:1909.11451v1 [physics.app-ph] 25 Sep 2019
I. INTRODUCTION

The central nervous system of the human body forms a critical signaling network that controls over 200 muscles. Understanding and measuring the nerve-innervation patterns and muscle activity controlled by this network is crucial for research, diagnosis and treatment of motor-system diseases like Parkinsons disease and amyotrophic lateral sclerosis (ALS). Recently, transcranial magnetic stimulation (TMS) has gained widespread use for the research and diagnosis of various neuropsychiatric disorders. In TMS, a strong pulse of magnetic field can be applied to different cortical areas. When applied to the motor cortex, TMS results in an evoked muscle response in the form of a ‘twitch’. TMS offers a safe, controlled, and non-invasive method to investigate the motor pathways, making it an ideal platform for studying central motor conduction activity. Electrophysiological measurement techniques such as electromyography are used as a standard tool to study neural and muscle activity for peripheral intervention as achieved by descending motor waves evoked by TMS. During an electromyogram, surface or needle electrodes record differences in electric potential in periphery limbs, but the magnetic signals that accompany electrophysiological signals can provide additional crucial clinical information about innervation and muscle activity that is spatially and temporally well resolved.

The benefit of combining TMS with biomagnetic measurements is significant. Surface electrical potential measurements require electrodes placed on the skin, and therefore measure signals originating on or just below the surface. Magnetic fields, in contrast, can arise due to muscle activity at all depths, and mapping measurements of the field can be used to locate these sources. Since the relative magnetic permeability of human tissue is close to unity, the magnetic fields are directly related to the electro-chemical activity within muscles, unaffected by the surrounding biomass. Therefore, these magnetic signals are powerful tools for studying the proper functioning and response of the central nervous system, forming a crucial complement to both needle and surface electrode measurements, which measure relative electrical potential differences.

Additionally, since the detection of magnetic fields does not require physical contact, in contrast to surface or needle based electric potential measurements, magnetic measurements of muscle activity, or, magnetomyography (MMG) is a non-invasive and non-contact technique. These aspects make MMG an attractive tool for quantifying peripheral muscle activity, since it can detect magnetic signals from skeletal muscles with high spatial accuracy and with less discomfort for patients. Because TMS is a repeatable and controlled stimulation, measurements can be triggered and...
averaged with high accuracy in timing, improving the signal-to-noise ratio and repeatability of biomagnetic signals. Despite the apparent motivations for magneto-physiological measurements, the very small signal size (<10 pT) has limited widespread adoption of biomagnetic measurements as a routine clinical measurement, since this regime of sensitivity has been limited to SQUIDs (superconducting quantum interference devices), which require liquid helium cooling. As a result, while SQUIDs have been for decades used for detection of biomagnetic signals, the associated measurement systems are bulky, expensive, and ill-suited to the different geometries of various body parts, limiting these systems practical utility. Recent developments in atomic magnetometry have led to new, high-sensitivity devices known as optically pumped magnetometers (OPMs) that are uncooled, centimeter-scale, and relatively low cost - characteristics necessary to make magneto-physiological measurements an accessible diagnostic tool. Additionally, OPMs have opportunities and applications in wearable compact devices with wide application outside of clinical use. For these reasons, OPMs have recently generated broad research interest as a viable alternative to SQUIDs in measuring weak biomagnetic signals.

In this work, we leverage the advances in OPM technology to enhance the diagnostic utility of TMS. We combine an extended array of OPMs around the hand of a human subject with a surface electromyograph to provide a comparison of techniques. We also incorporate simultaneous electroencephalography (EEG) during measurements, and signals from the three detection systems can be compared. Finally, we achieve the above stated goals in a hospital exam room, using a portable magnetic shield that only encompasses the arm of the subject. This circumvents the need for a large and expensive magnetically shielded room. We show biomagnetic signals with features that are not present in EMG measurements. These results show an investigation of OPM-recorded evoked muscle activity from repetitive TMS, with the realization of local magnetic shielding for human biomagnetic measurements in a clinical setting. This OPM-TMS platform also opens new possibilities for identifying nerve transmission pathways and external detection of voluntary motor responses, a crucial step towards interfacing wearable technology with the human nervous system.

II. METHODS

A. Subjects

All measurements were repeated for four healthy subjects in total, between ages 26 and 40, who volunteered for the study and signed informed consent. All subjects are right-handed and have no severe somatic diseases or any mental or neurological diseases with confirmed diagnosis.

B. Experimental procedure

The OPM and EMG electrode configurations within the shield are shown in Figure 1a-b. The measurement preparation time, including control measurements, takes less than 30 minutes. The biomagnetic signal is recorded with an array of four OPMs below the hand and an additional four above the hand, while the EMG and EEG are simultaneously recorded to correlate and provide reference for the signals.

For each participant, the three sensing systems (magnetomyography magnetometers, EMG surface electrodes, and EEG electrodes) were prepared and tested individually with the data acquisition system. The EEG and EMG were recorded using the 128-channel EGI (Electrical Geodesics, Inc.) EEG system and synchronized with OPMs using a trigger signal from the TMS pulse. The subjects hand was positioned in the shield, and the TMS coil was positioned over the subjects left M1 region (Fig. 1c). The stimulation was applied at different frequencies 0.5 Hz, 3 Hz, and 9 Hz for a maximum of up to 3 min depending on the comfort of the subject.

The TMS pulse results in a ≈1.4 T field on the motor cortex of the participant, which is less than a meter away from the EMG and MMG sensor positions. The sensors record a magnetic artifact arising from the TMS pulse, which consists of a bi-phasic pulse lasting approximately 60µs. To identify and isolate this artifact, a control measurement was performed in which each participant moved his or her head down (Fig. 1h) and data was taken for same stimulation described above. Since the high-intensity region of the magnetic field from the TMS is highly localized, the participants change in head position results in there being no discernible evoked effect. No MEP is observed on the EMG, and a lack of finger ‘twitch’ was confirmed using a camera aimed through an access port on the shield. These measurements showed that this artifact lasts up to 15 ms on the averaged OPM signal.
C. Transcranial magnetic stimulation (TMS)

To administer TMS, a stimulation coil is placed over the target area of a participant's scalp, and a strong electrical current running through the coil results in a region of intense magnetic field within the participant's brain. This pulsed magnetic field induces a secondary electrical current within the cortical tissue, which, if within the motor cortex, may result in muscular activation\textsuperscript{28}. The muscle activity can be detected via electromyography, and the resulting signal is known as a motor-evoked potential (MEP)\textsuperscript{29}.

The Magstim Super Rapid 2 stimulator (Magstim, UK) with a figure-of-eight coil with internal wing diameter of 70mm was used. The TMS pulse had a bi-phasic waveform and was applied at the left primary motor cortex (M1) with an intensity of 110% of the subject's resting motor threshold (RMT) (Fig. 1c). The RMT was determined as the minimum stimulus intensity required to elicit motor evoked potentials of amplitude 50µV in 5 out of 10 consecutive trials at rest in the contralateral first dorsal interosseous muscle (Figure 1e)\textsuperscript{12,13}.
D. Optically pumped magnetometry in a portable shield

Detection of biomagnetic signals requires magnetic sensitivities better than 1 pT/√Hz. The commercially available OPMs (Quspin) used in this work can achieve a noise floor of 15 fT/√Hz with a bandwidth between 1 - 100 Hz. These sensors operate by optically probing the zero-field resonance of spin-polarized Rubidium atoms, which is highly sensitive to small magnetic fields.

The drawback of this magnetometry approach is a limited dynamic range, requiring a magnetically compensated or shielded background environment in order to reach the sensitivity limits, especially when considering a magnetically hostile hospital setting. Previous human biomagnetic measurements using OPMs were, for the most part, conducted in magnetically shielded rooms (MSRs) which typically have residual fields of < 10 nT, magnetic gradients on the order of 1 nT/m, and enough space to comfortably accommodate a subject. These characteristics constitute an appropriate working environment for OPMs, allowing low noise measurements and some freedom to move the sensors by 1-2 cm. However, MSRs are expensive and decidedly not portable, which ultimately restricts the OPM technology to the same limitations as SQUID devices. Furthermore, the isolated MSR environment can be unsuitable for subjects to remain inside for long measurement times. Importantly, the large magnetic field generated by TMS could magnetize and negatively affect the shielding.

To circumvent these practical issues associated with MSRs, we instead use a small-sized shield that encompasses only the body part relevant to the measurement. Since we are measuring nerve and muscle activity in the hand, the arm of the subject is placed inside a commercially available four-layer cylindrical shield (Twinleaf MS-2) with one set of end-caps removed. The missing end-cap compromises the DC shielding factor by about a factor of 10 within the sensor region, however, DC magnetic field offsets (<50 nT at sensor positions) arising in the shield can be compensated for with sensor compensation coils. Nevertheless, the open-shield modification makes the low-field region susceptible to environmental magnetic noise, therefore the ability to average over multiple trials is crucial for retaining a high SNR.

Since magnetic-field gradients can be relatively large with an open shield, the sensors must be protected from vibrations or any movement, particularly those that may accompany the invoked muscle activity. Therefore, the subject rests his or her arm on a custom plastic mold (shown in Fig. 2a-b) which is suspended from an aluminum support that extends into the shielded region, but is otherwise disconnected from the shield and sensors. The subject is thus able to make small movements within the shield without physical disturbance to the sensors and causing false signals. This was verified using control measurements in which the suspended mold and mount were moved at the expected trigger frequency without a subject arm inside.

Environmental magnetic changes in a hospital setting were measured using a fluxgate magnetometer placed outside the shield (Fig. 1b), and while large features (>100 nT on fluxgate) were visible on the OPMs, these artifacts were sufficiently shielded as to not cause the sensor output to go out of range during the measurement. The effects of these low-frequency transient offsets can be minimized by subtracting sensor signals (software gradiometry) and through averaging.

Eight commercial OPM sensors (Quspin) are used. Each sensor has two magnetically sensitive axes with separate outputs, resulting in a total of 16 magnetic sensor channels.

Relevant photographs of the experimental equipment and setup are shown in Fig. 2.

E. Electroencephalography and electromyography

The EEG signals were recorded with a high-density (256 electrodes) EEG system (Net Station 5.0, EGI, USA). The caps were placed manually with the Cz electrode positioned over a centralized location on the scalp, which was determined as the simultaneous midpoint of the arc length for both nasion-inion and preauricular arcs. The electrode impedances were kept under 50 K throughout the experiment, and a sampling frequency of 1000 Hz was applied. The surface EMG was recorded from the FDI muscles. Both the EEG and EMG were digitized by a single amplifier. The amplifier applies a bandpass filter (low frequency cutoff = 0.1 Hz, high frequency cutoff = 70 Hz), and notch filter (50 Hz) to the EEG. Similarly, a bandpass filter (low frequency cutoff = 0.5 Hz, high frequency cutoff = 120 Hz), and notch filter (50 Hz) were applied to the EMG.

F. Data analysis

All of the magnetometer data from each participant were analyzed using a custom Python code for cutting and averaging based on the TMS trigger signal. Notch filters were applied at 50 Hz (Q=20) and higher harmonics, and the data
FIG. 3. Combined EEG, EMG and MMG data for a single participant, showing relative detail in magnetic vs. electric myography, and how the data from three input methods in the experimental system complement each other. (a) 120 averages of MMG and EMG data before, during and after the TMS pulse (occurring at 0.0 s). Following the large artifact at the TMS pulse, magnetic activity in the hand is detected for approximately 300 ms in this subject. (b) Zoom of the data in (a) for the time period immediately following the TMS pulse. The magnetic sensors detect both activities which coincides with the electric channel, and which occurs while the electric channel shows nothing. Four of 16 magnetic sensor channels were selected based on noise levels and signal amplitude. Referencing Fig. 1: MMG1, magnetometer 90; MMG2, magnetometer AB. (c) EEG topograms of brain activity during selected points after the TMS pulse. The topograms were analyzed at times where magnetic features had largest amplitude. Brain activity begins in the motor cortex where the TMS pulse is applied. The activity then moves to other regions of the brain over the course of the measurement.

were smoothed with an evenly weighted four-point moving window. The EMG electrode data were extracted and partially analyzed using MNE, an open-source Python software.\textsuperscript{24,25} The TMS-evoked potentials (TEP) were computed from the analysis of EEG data using Matlab 2015b and the Fieldtrip toolbox (http://www.fieldtriptoolbox.org/). The exact details of the pre-processing steps and analysis have been described elsewhere\textsuperscript{26}. To establish the robustness of the latency values across trials, a set number of trials were selected at random to be averaged, and a double Gaussian fit with linear offset was made around 25 ms after the trigger on a single channel. This time window was chosen to coincide with the MEP latency. The double Gaussian was chosen as best able
FIG. 4. Combined MMG, EMG, and EEG data for four participants. Variability across subjects is clearly discernible in the MMG data, but all show qualitatively similar results for all signal types. The shape of the TMS artifact is strongly dependent on the position of the coil relative to the magnetic shield, which varies from participant to participant. Additionally, the actual duration of the TMS pulse is \( \approx 60\) µs, while the data acquisition rate is 1kHz, resulting in aliasing of the TMS artifact, which reduces its size after averaging. Note: The EMG electrode from Subject 1 was found afterwards to have been improperly grounded, leading to large noise artifacts that remained after filtering and smoothing. Nevertheless, the MEP is still visible.

III. RESULTS AND DISCUSSION

Averaged data resulting from 120 repetitive TMS pulses at 0.5 Hz in a single participant are shown in Figure 3. While 16 magnetic sensor channels are available from the experiment, we select the four shown for clarity and consistency across subjects because some sensors failed (out of range due to environment) during measurements. The sensors shown [y- and z- axes from magnetometers MMG1(9O) and MMG2(AB)] are positioned below and above the hand, respectively. The signals arising from other sensors are qualitatively similar. In Figure 3, the signals from both the EMG and MMG are shown to occur within 300 ms of the TMS pulse, with little discernible activity thereafter. During the TMS magnetic artifact, the y and z sensors record large features with the same sign, indicating that fields at these sensors are aligned similarly.

Figure 3b shows a narrower time window. Here, both magnetic and electric (shown in red) channels exhibit a
FIG. 5. Robustness of latency of magnetic peak recorded near EMG action potential for subject number 4. (a) Calculated latency vs number of averages. Latency is calculated by averaging fixed number of random trials and then fitting the magnetic signal data to a bi-phasic peak and extracting the center offset. Latency value falls within 1 standard deviation of final value within 45 averages. (b) Example double gaussian fit of a 100 trials of magnetic signal from a single channel to find the latency. Latency is defined as 2.5\( \sigma \) prior to the center offset fit of the first gaussian, where \( \sigma \) is the half-width-half-max.

feature at 26 ms, which can be understood as the time for a nerve signal to travel from the motor cortex to the hand. On the EMG channel, this feature is identified as the MEP \( [12] \). On the MMG channel, the relative sign and shapes of the magnetic features in the data could be used to inform source location of the muscle activity. Starting at around 50 ms after the TMS pulse, the magnetic channels record a bi-phasic feature that lasts up to 200 ms. This larger magnetic signal does not appear on the EMG. The loss of this H-reflex signal in EMG recording could be due to the choice of filter parameters implemented in this study \( [36] \).

The MMG data is used to identify time points after the TMS pulse at which to examine the EEG topology plots, shown in Figure 3c. At the topology plot data at 26 ms, corresponding to the time of the MEP, electrical activity in the brain was observed at the location of the TMS stimulus, in the M1 region. At later times, 86 ms and 180 ms, this activity moved to contralateral M1, and parietal regions respectively. Furthermore, the results showed similar patterns in other subjects. These results show that TMS induces focal effects, and that these effects spread to other brain regions beyond the stimulated region \( [37] \).

Figure 4 shows the TMS invoked magnetic and electric response of the hand for four subjects. Each subject has a unique magnetic signal - for example, data from Subject 1 shows magnetic field values that are almost three times as large as those of the other subjects. Inter-subject variability during TMS could account for variability in the EMG and MMG recording \( [38] \). For both EMG and MMG, variability was calculated by removing any constant or linear offsets from the signal and summing the absolute values between the TMS trigger and 500 ms post trigger, calculating the effective area below the signal curves. The variation from the mean (VFM) value of the area is calculated and the average variability for all four subjects is 28\% for EMG recordings, and 34\% for MMG recordings. Variability in the magnetic recordings is greater than that of the EMG, which could result from the fact that the magnetic signal is strongly dependent on the distance between source and sensor, which varied based on the subject physiology. Inter-trial variation could not be calculated because of inadequate signal-to-noise-ratio.

Data from all the participants show that the MEP from the EMG is detected in the magnetometer channels. Finally, in the EEG we observe qualitatively similar behavior of the brain activity across subjects at the time points chosen based on features in the MMG.

The robustness in calculating the latency of MEP in the MMG signals is shown in Figure 5. Figure 5a shows that the value for the latency settles to within one standard deviation of the final calculated value (maximum number of averages) within 45 averages. This analysis was used for all subjects.

While there is good agreement between the latencies extracted from MMG or EMG measurements (Table 1), the magnetic field measurement holds several benefits over the electrical potential measurement. MMG is more reliable and repeatable for comparing the strength of the signal, since magnetic field strength is not influenced by the tissue or bone, and thus accurately conveys the absolute value of the field from the source. In contrast, the EMG data can be influenced by several factors including poor skin contact, residual limb sweating, and their ability to only record signals from superficial muscles, whose function frequently does not relate to the intended movement. Furthermore, quantitative analysis of relative electrical potential measurements is not feasible, whereas the magnetic field data can be used to perform source location given a model of the nerve or muscle activity.
TABLE I. Comparison of MEP latency from EMG vs. MMG for each subject. Error, shown in parentheses, was calculated from covariance matrix of the fitted Gaussian function. Error for average is standard deviation of the four subjects. For Subject 4, there is a 1σ discrepancy in the timing of the MEP as measured from electric and magnetic channels. The good agreement in the averages indicates that there is no statistically significant systematic over- or under-reporting of one method relative to the other.

| Subject | MMG [ms] | EMG [ms] |
|---------|----------|----------|
| 1       | 26(1)    | 25(1)    |
| 2       | 20(2)    | 20(1)    |
| 3       | 18(2)    | 19(2)    |
| 4       | 22(1)    | 20(1)    |
| Average | 22(3)    | 21(2)    |

IV. CONCLUSION

These first results of OPM-recorded magnetic signals from TMS-evoked movement demonstrate the viability of the TMS-OPM system for clinical research. The combined use of magnetic and electric field sensors allows for detailed discrimination of different signals, while providing complementary information about muscle activity in the hand. TMS is targeted, repeatable and safe, and thus can be used in a future study to identify the innervation pathways for specific muscles in various locations along the arm, by using the magnetic data for source location.

Together with the arm-sized magnetic shield, we show how commercial OPM systems can enhance the utility of TMS. The magnetic field data offers complementary information to electrical potential data, and the portable and economical aspects of OPMs (as compared to SQUIDs) makes TMS-OPM a viable clinical tool. This approach represents a new modality in TMS research with opportunities for peripheral nerve study. Additionally, future implementations of this system within head sized shields will enable low-cost and accessible magnetoencephalography, furthering research towards better understanding and diagnoses of movement disorders and motor neuron diseases.

V. AUTHOR CONTRIBUTIONS

G.Z.I., Y.H., conceived of, designed, and constructed the apparatus. Y.H., G.Z.I., T.S., M.M., and V.C.C. prepared and performed the experiments. G.Z.I., Y.H., M.M., and V.C.C. analyzed the data. G.Z.I., M.M., and V.C.C. wrote the manuscript. M.M and S.G. advised and informed clinical aspects of the work. M.M, S.G., D.B., and A.W. supervised the work.

VI. COMPETING INTERESTS

The authors declare no competing interests.

VII. ACKNOWLEDGEMENTS

The work was funded in part by the German Federal Ministry of Education and Research (BMBF) within the Quantumentechnologien program (FKZ 13N14439) and the Deutsche Forschungsgemeinschaft (DFG) through the DIP program (FO 703/2-1) and the Other Instrumentation-Based Research Infrastructure program (FKZ 324668647). S.G acknowledges support from the Transregional Collaborative Research Center (CRC) TR-128.

REFERENCES

1. S. Wynter and L. Dissabandara, “A comprehensive review of motor innervation of the hand: variations and clinical significance,” Surgical and Radiologic Anatomy 40, 259–269 (2018).
2. S. Vucic, D. Burke, and M. Kiernan, “The motor neuron disease handbook,” (2007).
3. J. M. Winhammar, D. B. Rowe, R. D. Henderson, and M. C. Kiernan, “Assessment of disease progression in motor neuron disease,” The Lancet Neurology 4, 229–238 (2005).
4 S. Vucic, U. Ziemann, A. Eisen, M. Hallett, and M. C. Kiernan, “Transcranial magnetic stimulation and amyotrophic lateral sclerosis: pathophysiological insights,” J Neurol Neurosurg Psychiatry 84, 1161–1170 (2013).

5 Y.-h. Chou, P. T. Hickey, M. Sundman, A. W. Song, and N.-k. Chen, “Effects of repetitive transcranial magnetic stimulation on motor symptoms in parkinson disease: a systematic review and meta-analysis,” JAMA neurology 72, 432–440 (2015).

6 R. Cantello, R. Tarletti, and C. Civardi, “Transcranial magnetic stimulation and parkinsons disease,” Brain research reviews 38, 309–327 (2002).

7 P. Rossini, A. Berardelli, G. Deuschl, M. Hallett, A. Maertens de Noordhout, W. Paulus, and F. Pauri, “Applications of magnetic cortical stimulation,” Electroencephalogr Clin Neurophysiol Suppl 52, 171–185 (1999).

8 M. Kobayashi and A. Pascual-Leone, “Transcranial magnetic stimulation in neurology,” The Lancet Neurology 2, 145–156 (2003).

9 M. Hallett, “Transcranial magnetic stimulation and the human brain,” Nature 406, 147 (2000).

10 S. M. Goetz and Z.-D. Deng, “The development and modelling of devices and paradigms for transcranial magnetic stimulation,” International Review of Neurology 29, 115–145 (2017).

11 P. M. Rossini and S. Rossi, “Transcranial magnetic stimulation: diagnostic, therapeutic, and research potential,” Neurology 68, 484–488 (2007).

12 S. Groppa, A. Oliviero, A. Eisen, A. Quartarone, L. G. Cohen, V. Mall, A. Kaelin-Lang, T. Mima, S. Rossi, G. W. Thickbroom, P. M. Rossini, U. Ziemann, J. Valls-Solé, and H. R. Siebner, “A practical guide to diagnostic transcranial magnetic stimulation: report of an ifcn committee,” Clin Neurophysiol 123, 858–882 (2012) 22349304[pmid]

13 R. McMackin, M. Muthuraman, S. Groppa, C. Babiloni, J.-P. Taylor, M. C. Kiernan, B. Nasseroleasmani, and O. Hardiman, “Measuring network disruption in neurodegenerative diseases: New approaches using signal analysis,” Journal of Neurology, Neurosurgery & Psychiatry 90, 1011–1020 (2019).

14 L. G. Tassinary, J. T. Cacioppo, and E. J. Vanman, “The skeletonmotor system: Surface electromyography,” in Handbook of psychophysiology, edited by J. T. Cacioppo, L. G. Tassinay, and G. G. Berntson (Cambridge University Press, New York, NY, 2007) pp. 267–299.

15 D. Cohen and E. Givler, “Magnetomyography: Magnetic fields around the human body produced by skeletal muscles,” Applied Physics Letters 21, 114–116 (1972).

16 T. Masuda, H. Endo, and T. Takeda, “Magnetic fields produced by single motor units in human skeletal muscles,” Clinical neurophysiology 110, 384–389 (1999).

17 J. C. Mosher, P. S. Lewis, and R. M. Leahy, “Multiple dipole modeling and localization from spatio-temporal meg data,” IEEE transactions on biomedical engineering 39, 541–557 (1992).

18 J. F. Schenck, “The role of magnetic susceptibility in magnetic resonance imaging: MrI magnetic compatibility of the first and second kinds,” Medical physics 23, 815–850 (1996).

19 S. J. Williamson, G.-L. Romani, L. Kaufman, and I. Moden, Biomagnetism: an interdisciplinary approach, Vol. 66 (Springer Science & Business Media, 2013).

20 H. Weinstock, SQUID sensors: fundamentals, fabrication and applications, Vol. 329 (Springer Science & Business Media, 2012).

21 D. Grimes, R. Lennard, and S. Swithenby, “Dc magnetic fields of the human leg as a function of position and relaxation,” Il Nuovo Cimento D 5, 650–659 (1983).

22 D. Drung, “The ptb 83-squid system for biomagnetic applications in a clinic,” IEEE transactions on applied superconductivity 5, 2112–2117 (1995).

23 M. Burghoff, H. H. Allbrecht, S. Hartwig, I. Hilschenz, R. Köhrer, T. Sander-Thömmes, H. Scheer, J. Voigt, and L. Trahms, “Squid system for meg and low field magnetic resonance,” Metrol. Meas. Syst 16, 650–659 (2009).

24 J. Allred, R. Lyman, T. Kornack, and M. Romalis, “High-sensitivity atomic magnetometer unaffected by spin-exchange relaxation,” Physical review letters 89, 130801 (2002).

25 E. Boto, N. Holmes, J. Leggett, G. Roberts, V. Shah, S. S. Meyer, L. D. Muñoz, K. J. Mullinger, T. M. Tierney, S. Bestmann, et al., “Moving magnetoencephalography towards real-world applications with a wearable system,” Nature 555, 657 (2018).

26 G. Gonzalez-Escamilla, V. C. Chirumamilla, B. Meyer, T. Bonertz, S. von Grothhus, J. Vogt, A. Stroh, J.-P. Horstmann, O. Tüscher, R. Kalisch, et al., “Excitability regulation in the dorsomedial prefrontal cortex during sustained instructed fear responses: a tms-eeg study,” Scientific reports 8, 14506 (2018).

27 P. J. Broser, S. Knappe, D.-S. Kajal, N. Noury, O. Alem, V. Shah, and C. Braun, “Optically pumped magnetometers for magneto-emyography to study the innervation of the hand,” IEEE Transactions on Neural Systems and Rehabilitation Engineering 26, 2226–230 (2018).

28 R. Cavaleri, S. M. Schabrun, and L. S. Chipchase, “The number of stimuli required to reliably assess corticomotor excitability and primary motor cortical representations using transcranial magnetic stimulation (tms): a systematic review and meta-analysis,” Syst Rev 6, 48–48 (2017), 28264713[pmid].
29. A. Barker, R. Jalinous, and I. Freeston, “Non-invasive magnetic stimulation of human motor cortex,” The Lancet, 325, 1106 – 1107 (1985), originally published as Volume 1, Issue 8437.
30. V. K. Shah and R. T. Wakai, “A compact, high performance atomic magnetometer for biomedical applications,” Physics in Medicine & Biology 58, 8153 (2013).
31. E. Boto, S. S. Meyer, V. Shah, O. Alem, S. Knappe, P. Kruger, T. M. Fromhold, M. Lim, P. M. Glover, P. G. Morris, et al., “A new generation of magnetoencephalography: Room temperature measurements using optically-pumped magnetometers,” NeuroImage 149, 404–414 (2017).
32. G. W. Sullivan, P. Lewis, J. George, and E. Flynn, “A magnetic shielded room designed for magnetoencephalography,” Review of Scientific Instruments 60, 765–770 (1989).
33. T. C. Ferree, P. Luu, G. S. Russell, and D. M. Tucker, “Scalp electrode impedance, infection risk, and eeg data quality,” Clinical Neurophysiology 112, 536–544 (2001).
34. A. Gramfort, M. Luessi, E. Larson, D. A. Engemann, D. Strohmeier, C. Brodbeck, R. Goj, M. Jas, T. Brooks, L. Parkkonen, et al., “Meg and eeg data analysis with mne-python,” Frontiers in neuroscience 7, 267 (2013).
35. A. Gramfort, M. Luessi, E. Larson, D. A. Engemann, D. Strohmeier, C. Brodbeck, L. Parkkonen, and M. S. Hämäläinen, “Mne software for processing meg and eeg data,” Neuroimage 86, 446–460 (2014).
36. A. Christie, G. Kamen, J. P. Boucher, J. Greig Inglis, and D. A. Gabriel, “A comparison of statistical models for calculating reliability of the hoffmann reflex,” Measurement in Physical Education and Exercise Science 14, 164–175 (2010).
37. M. M. Shafi, M. B. Westover, M. D. Fox, and A. Pascual-Leone, “Exploration and modulation of brain network interactions with noninvasive brain stimulation in combination with neuroimaging,” European Journal of Neuroscience 35, 805–825 (2012).
38. L. Kiers, D. Cros, K. Chiappa, and J. Fang, “Variability of motor potentials evoked by transcranial magnetic stimulation,” Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section 89, 415–423 (1993).