Brain Stimulation xxx (2017) 1–9

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Where and what TMS activates: Experiments and modeling

Ilkka Laakso [a, *], Takenobu Murakami [b, c], Akimasa Hirata [d], Yoshikazu Ugawa [b, c]

[a] Department of Electrical Engineering and Automation, Aalto University, Espoo, Finland
[b] Department of Neurology, Fukushima Medical University, Fukushima, Japan
[c] Fukushima Global Medical Science Center, Advanced Clinical Research Center, Fukushima Medical University, Fukushima, Japan
[d] Department of Computer Science and Engineering, Nagoya Institute of Technology, Nagoya, Japan

ARTICLE INFO

Article history:
Received 3 March 2017
Received in revised form
22 June 2017
Accepted 22 September 2017
Available online xxx

Keywords:
Transcranial magnetic stimulation
Motor cortex
Motor evoked potentials
Finite element analysis
Computer simulation
Patient-specific modeling

ABSTRACT

Background: Despite recent developments in navigation and modeling techniques, the type and location of the structures that are activated by transcranial magnetic stimulation (TMS) remain unknown.
Objective: We studied the relationships between electrophysiological measurements and electric fields induced in the brain to locate the TMS activation site.
Methods: The active and resting motor thresholds of the first dorsal interosseous muscle were recorded in 19 subjects (7 female, 12 male, age 22 ± 4 years) using anteromedially oriented monophasic TMS at multiple locations over the left primary motor cortex (M1). Structural MR images were used to construct electric field models of each subject's head and brain. The cortical activation site was estimated by finding where the calculated electric fields best explained the coil-location dependency of the measured MTs.
Results: The experiments and modeling showed individual variations both in the measured motor thresholds (MTs) and in the computed electric fields. When the TMS coil was moved on the scalp, the calculated electric fields in the hand knob region were shown to vary consistently with the measured MTs. Group-level analysis indicated that the electric fields were significantly correlated with the measured MTs. The strongest correlations ($R^2 = 0.69$), which indicated the most likely activation site, were found in the ventral and lateral part of the hand knob. The site was independent of voluntary contractions of the target muscle.
Conclusion: The study showed that TMS combined with personalized electric field modeling can be used for high-resolution mapping of the motor cortex.

© 2017 Elsevier Inc. All rights reserved.

Introduction

Transcranial magnetic stimulation (TMS) can non-invasively activate the motor cortex, evoking measurable muscle responses; this is useful for investigating the function of the motor cortex and its descending pathways. Depending on the stimulation parameters, such as the stimulation intensity, magnetic coil orientation, and stimulation waveform, TMS selectively activates different neural elements, producing descending corticospinal waves with variable amplitude and latency [1,2]. However, the type and location of the activated neural structures and the spatial extent of TMS-induced activation in the brain remain unclear.

In experimental studies, the activation site of TMS is conventionally estimated by finding the scalp location that generates the strongest response in a target muscle and projecting this location to the cortical surface [3,4]. However, this approach is flawed, because it does not account for the influence of the individual anatomy of the brain and head on the electric (E) fields induced by TMS. Recent numerical modeling studies have shown that accurate representation of the brain anatomy is necessary to make specific predictions of the TMS target areas [5–7]. However, TMS induces E-fields distributed over large parts of the motor cortex and surrounding areas, making it difficult to determine where the activation occurs, even when detailed anatomical models are used.

The objective of this study was to find the activation site both in individual brains and in the standard brain space. We based our investigation on TMS motor threshold (MT) measurements at multiple scalp sites in multiple individuals. The induced E-fields

* Corresponding author. Aalto University, Otakaari 3, 02150 Espoo, Finland.
E-mail address: ilkka.laakso@aalto.fi (I. Laakso).

https://doi.org/10.1016/j.brs.2017.09.011
1935-861X/© 2017 Elsevier Inc. All rights reserved.

Please cite this article in press as: Laakso I, et al., Where and what TMS activates: Experiments and modeling, Brain Stimulation (2017), https://doi.org/10.1016/j.brs.2017.09.011

were modeled based on individual MR images and were specific to each individual.

Materials and methods

Subjects

Nineteen healthy right-handed subjects (7 female, 12 male, age 22 ± 4 years) participated in the study. None of the participants had any contraindications to TMS, took any medication on a regular basis, or had a positive history of psychiatric or neurological diseases [8]. All subjects provided written informed consent to participate in this study. The study was approved by the local ethics committee of Fukushima Medical University.

Imaging

Structural T1-and T2-weighted MRI scans were acquired using a 3 T MRI scanner (Siemens Biograph mMR) with the following parameters: T1 MPRAGE sequence with TR/TE/TI/FA/FOV/voxel size/slice number = 1800 ms/1.99 ms/800 ms/9°/256 mm/0.976 mm × 0.976 mm × 1.0 mm/176, and T2 with TR/TE/FOV/voxel size/slice number = 3200 ms/361 ms/256 mm/0.488 mm × 0.488 mm × 1.0 mm/176.

Electromyography

Electromyograms (EMGs) were recorded from the right first dorsal interosseous (FDI) muscle using pairs of Ag-AgCl surface electrodes in a belly-tendon montage. The raw signals were amplified and bandpass filtered (100 Hz–3 kHz, Multi Amplifier 1000, DIGITEX LAB Co. Ltd., Japan). The signals were digitized at 5 kHz and the data were stored on a computer for offline analysis (MultiStim tracer; Medical Try System, Japan).

Transcranial magnetic stimulation

Single-pulse TMS was applied with a figure-of-eight coil (70 mm diameter) connected to a monophasic Magstim 200^2 stimulator (Magstim Co. Ltd., UK). The stimulating coil was positioned tangentially to the skull with the coil handle pointing backwards and laterally at 45° from the anterior-posterior axis. The "motor hot spot" (HS) was determined as the site where TMS consistently elicited the largest motor evoked potentials (MEPs) from the right FDI muscle. The spot was marked on the scalp with a waterproof pen alongside the front edge of the TMS coil. The resting MT (RMT) was determined to the nearest 1% of the maximum stimulator output; it was defined as the lowest stimulus intensity that elicited a minimum MEP amplitude of 50 μV in the completely relaxed FDI muscle in at least 5 out of 10 consecutive trials [9]. The active MT (AMT) was defined as the minimum stimulator output intensity that evoked an MEP amplitude of at least 200 μV in 5 out of 10 trials while the subjects maintained 10% of their maximum voluntary contraction of the right FDI muscle.

In addition to the HS, up to four additional stimulation sites were marked on the scalp, located at anteromedial (AM), posterolateral (PL), posteromedial (PM), and anterolateral (AL) positions to the HS at a distance of 2 cm. In nine subjects (three female, age 21 ± 3 years), the measurements were conducted at five coil locations, and in the other ten subjects (four female, age 22 ± 5 years), the experiments were performed at three locations (HS, AM, and PL).

We note that our stimulation target was the neural structures that are activated by stimulation in the 45° direction, and are known to preferentially produce short-latency I1 waves [10–12].

Coil positioning

To perform the TMS experiments prior to obtaining MRI scans of each subject, a method was developed for the offline reconstruction of the coil location. The method was based on the calculation of the geodesic distances from several anatomical landmarks on a 3D surface model of the scalp surface (Fig. 1) and is described in Supplementary Note 1. The coil direction was not recorded because we estimated that it had a small impact on the E-fields (see Results).

Cortical reconstruction

The cortical surfaces were reconstructed from the MRI using the FreeSurfer image analysis software (version 5.3.0, available online at http://surfer.nmr.mgh.harvard.edu). The default values were used for all the parameters. Briefly, FreeSurfer uses the T1-weighted MRI as input and generates polygonal representations of the grey matter–CSF and white matter–grey matter surfaces [13–16].

Volume conductor models

The grey and white matter surfaces generated by FreeSurfer were voxelized in a grid with a resolution of 0.488 mm. Non-brain tissues were segmented from T1-and T2-weighted MRI using a semi-automatic procedure described previously [17].

The electrical conductivities (S/m) of the grey and white matter (0.26 and 0.17) were obtained from *in vivo* human measurements at 50 kHz [18]. These values were extrapolated to the frequency of 3 kHz of the magnetic stimulator [19] using a four Cole–Cole parametric model [20], obtaining 0.215 and 0.142, respectively. The conductivity of human CSF at body temperature was 1.79 based on measurements performed at a frequency of 3.33 kHz [21]. The conductivities of other tissues, which had negligible impact on the modeling results, were assigned the following values: compact and spongy bone 0.009 and 0.034 [22], respectively, (values increased 30% to compensate for room temperature measurements), subcutaneous fat and skin (dermis) 0.15 and 0.43, correspondingly [23], muscle 0.18 [24], dura 0.18 (assumed the same as muscle owing to the lack of data), and blood 0.7 [20].

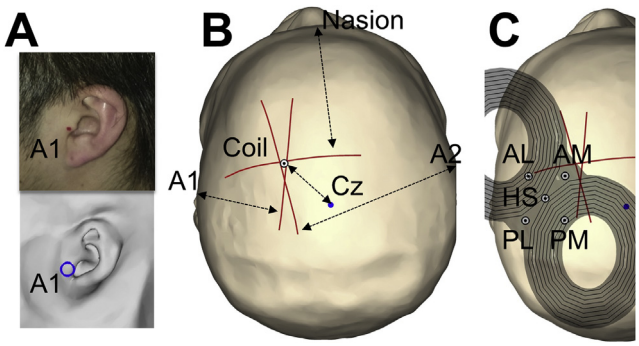

Fig. 1. TMS coil locations. A. Anatomical landmarks were photographed, and the photographs were used to determine the landmarks on a 3D model of the skin surface. B. The measured distances from the nasion and pre-auricular points were used to determine the vertex and coil locations. The front edge of the coil is at the intersection of the geodesic distance contours. C. The five coil locations used in the experiments and modeling.

Please cite this article in press as: Laakso I, et al., Where and what TMS activates: Experiments and modeling, Brain Stimulation (2017), https://doi.org/10.1016/j.brs.2017.09.011

Download English Version:

https://daneshyari.com/en/article/8681548

Download Persian Version:

https://daneshyari.com/article/8681548

Daneshyari.com