Non-invasive estimation of motor cortical functional anisotropy and muscle representation with neuronavigated transcranial magnetic stimulation

Petro Julkunen, Minna Pitkänen, Elisa Kallioniemi
Department of Clinical Neurophysiology
Kuopio University Hospital
Kuopio, Finland
petro.julkunen@kuh.fi

Petro Julkunen, Elisa Kallioniemi
Department of Applied Physics
University of Eastern Finland
Kuopio, Finland

Minna Pitkänen
Department of Neuroscience and Biomedical Engineering
Aalto University School of Science
Espoo, Finland

***Abstract*— Neuronavigated transcranial magnetic stimulation (nTMS) is a non-invasive brain stimulation method and it allows targeting TMS to specific cortical regions. This enables the application of nTMS to study motor-cortical somatotopy and to estimate the extent and location of cortical representation areas of muscles. The use of multichannel electromyography permits the stimulation triggered synchronous recording of muscle-specific responses to TMS. Therefore, motor function can be mapped for its extent and location using nTMS.**

In addition, the underlying cortical structure embedded with neuronal networks can be evaluated through a focal structure-function relation. Recently, nTMS has been used to evaluate cortical functional anisotropy for specific small hand muscles. The simple principle of the evaluation technique relies on the ability of TMS to activate neurons, which depends on the direction of the stimulated neurons. Ideally, if the neurons of the cortex possess similar directionality, the responses are induced with a narrow angle of coil rotation. Instead, if the neurons tend to have various directions, a larger coil orientation sector will produce the responses. Application of this principle provides the concept of functional anisotropy index (AI), which can be computed based on the use of various coil orientation angles at a stimulation target. The novel AI has been shown to link with the muscle-dependent level of cortical excitability.

Overall, bringing together the macroscopic cortical anatomy and muscle representation with nTMS enables a multi-scale estimation of cortical muscle-representations. These new measures can potentially be utilized e.g., for studying cortical stroke or when making pre-surgical evaluations on motor cortical representation areas.

Keywords—transcranial magnetic stimulation; motor cortex; motor evoked potential; anisotropy index; neuronavigation

I. Introduction

Neuronavigated transcranial magnetic stimulation (nTMS) is a non-invasive brain stimulation method [1], which can be used to map the extent and location of the cortical motor function [2] (Fig. 1). Use of real-time neuronavigation with TMS has made it possible to record the stimulus locations on the cortex in order to match a stimulation response with corresponding stimulus coordinates within the magnetic resonance imaging (MRI)-coordinate space. Our recent studies have utilized this capability to locate, outline and estimate representation size in a quantitative manner [2, 3].

TMS induces an electric field (EF) in the cortex which extends to neuronal bundles in several layers under the stimulation location [4]. Although the cortical excitability is influenced by physiological factors [5], we have observed that there is a connection between the cortical excitability and the underlying neuronal structure [6]. To evaluate this relation, i.e., cortical functional anisotropy, TMS is assumed to activate neuronal bundles parallel to the induced EF [7] and bundles having bends [4].

This paper focuses on introducing the novel aspects of the measurement of cortical functional anisotropy and representation size using nTMS.

II. Motor cortical mapping

By choosing whether TMS is timed during muscle relaxation or voluntary muscle contraction, it is possible to either excite muscle activity by inducing muscle responses or to inhibit voluntary muscle activity by evoking a silent period to the muscle contraction visible in the electromyography [3]. Thus, excitatory and inhibitory functions can be mapped for their extent and location.

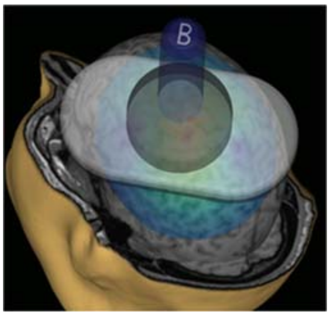

Fig. 1. A figure-of-eight TMS-coil placed on the scalp targeting the primary motor cortex. The coil and patient's MR-images have been co-registered.

When converting the stimulus locations from 3D space to 2D, cortical surface, the extent of the muscle representations can be computed based on spline interpolation streamlines or Voronoi tessellation for certain size responses [2]. We utilized this method to compare representations of inhibitory and excitatory responses in the proximity of the primary motor cortex. We found that the excitatory representations may be larger on the dominant hemisphere than on the non-dominant, while no inter-hemispheric difference exists with inhibitory representations. The excitatory representations tend to locate more medially and anteriorly compared to the inhibitory when assessed through activation centre-of-gravity [3].

The potential of cortical mapping to outline and measure cortical muscle representation size extends to patient populations. For example, patients preparing for respective tumor surgery may undergo a pre-surgical mapping procedure with nTMS, in which muscle representations close to the operated site are mapped for outlining functionally active sites (Fig. 2).

III. Functional Anisotropy

Based on the principles of electromagnetism and electrophysiology, TMS activates the neurons that are suitably oriented with respect to the stimulating EF [7,8]. Hence, TMS possesses the potential to evaluate the neuronal microstructure [6]. We recently developed a method utilizing nTMS to quantitatively evaluate the function and structure of the motor cortex concurrently [6,10]. The developed method measures a functional anisotropy index (AI), which is based on motor responses induced at different coil orientations. The AI has demonstrated association with both the motor cortex excitability and neuronal structure [6]. Further, the AI can be measured with good repeatability [10]. However, patient studies on AI have not been conducted so far, and therefore the final validation is still lacking.

IV. Conclusion

Our most recent findings and development on motor cortical mapping have demonstrated that novel quantitative and meaningful information can be gathered using nTMS. These methods can be integrated in clinical procedures to aid pre-surgical mapping procedures and stereotaxic radiosurgery planning [8,9]. In addition, conditions affecting the neuronal organization within the cortical structure can potentially be estimated based on AI, e.g. in cortical stroke. Overall, bringing the macroscopic cortical anatomy and muscle representation together with nTMS facilitates a multi-scale estimation of cortical muscle-representations.

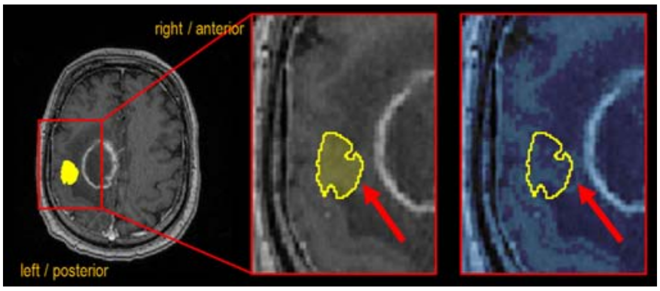

Fig. 2. Cortical representation areas of hand muscles outlined using nTMS and our assessment methods [2,3]. On the left hemisphere, the tumor is visible in the MRI (on the left). In the close-ups (in the middle), oedema surroungind the tumor has penetrated the functionally active cortical area (indicated by the red arrow), especially, when image contrast is enhanced (on the right).

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