Establishing standards for neuronavigated TMS in research and clinical studies

One of the main successes in the use of transcranial magnetic stimulation (TMS) in research and clinical neurophysiology is the ability to objectively characterize and modulate the functional state of brain regions and their connections. A functional characterization of the motor system can be achieved by measurements of the central-motor conduction time, amplitude or latency of the motor evoked potentials (also in relation to the maximum compound muscle action potential), motor threshold or recruitment curves. For both research and clinical practice an important aim is the establishment of precise and reliable measurement algorithms that closely reflect the functional state of the addressed system (Groppa et al., 2012).

Physiological fluctuations of the functional state make reliable measurements challenging. A number of factors such as oscillatory activity and excitability, and varying input-output balance of cortico-cortical and cortico-subcortical volleys might contribute to these fluctuations. For the precise characterization of the motor system the spinal excitability should be considered as well as important parameters that influence the functional state. In particular, the synchronization and de-synchronization of the corticospinal neurons and multiple discharges of the spinal motor neurons contribute to the variability of the physiological fluctuations. TMS can, however, reliably characterize the functional state of the motor system and cortico-spinal route if the methodological prerequisites are followed.

In this issue of Clinical Neurophysiology, Chang et al. (2016) address the question of the optimal number of pulses necessary to achieve reliable measures of the amplitude and latency of the motor evoked potentials (MEPs). The work is pertinent since it provides guidelines regarding the minimum number of pulses needed to achieve reliable MEP measurements in single and double-pulse paradigms. Studies on how many MEP trials should be recorded to optimally estimate the MEP amplitude and latency are lacking. In the recent IFCN Guidelines we recommend for clinical studies to focus only on the best 5–6 consecutive motor responses with the largest amplitude and the shortest latency; a strategy that provides an estimate of the optimal corticomotor conduction and a compromise between the duration of investigation and the sought accuracy, making optimization and standardization of the measurements for each laboratory mandatory.

The authors analyzed the mean MEP amplitude as strategy for the calculation of the number of pulses needed to acquire a reliable estimate of MEPs. The minimum number of pulses needed to achieve reliable amplitude and latency MEPs measures was shown to be 21 and 23, respectively. Another strategy could have been the use of weighted pooling of the MEPs amplitude and latency instead of a simple mean. This would have given more weight to the trials with the higher MEP amplitude and latency which will possibly further improve the reliability measurements and the proper characterization of the physiological correlate.

Additionally, the variability in the MEP parameters across trials and subjects could have been considered for the standardization. Therefore, the standard deviation of MEPs amplitude and latency measurements could have been further analyzed by i.e. the aid of Bayesian statistics (Kruschke, 2013). The Bayesian power analyses can be used to test the number of measurements required for achieving reliable results. The advantages of this method are that the data need not to be normally distributed; second, there is no need to apply corrections for multiple testing; and finally the test can be also applied for smaller sample sizes.

This work proposes guidelines for neuronavigated TMS of the motor cortex. A direct comparison of navigated and non-navigated TMS was not done, while previous work on this issue exists (Siebner et al., 2009; Sparing et al., 2008). Through the use of navigated TMS alterations of the spatial accuracy are controlled. In the motor system small variations of the stimulation site are reflected in clear changes of MEP latency and amplitude, while a physiological readout to TMS of other cortical regions does not yet exist. The quantification of the functional state or excitability changes through EEG could overcome this lack of a neurophysiological correlate with TMS of cortical areas other than the motor cortex (Groppa et al., 2013). An important question would be if the guidelines proposed in this study would apply to TMS-EEG recordings as well. The integrative analysis of MEP and TMS–EEG evoked potentials variability could bring up important insights and differentiate cortical and spinal excitability fluctuations.

Furthermore, this study has possibly taken the first essential steps towards the standardization of multi-center TMS studies. Established standards for hardware, setup and analysis algorithms could improve the reliability of measurements across equipment and laboratory settings and facilitate multisite-center studies with the same protocol to generalize the results.

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