Biomedical Physics & Engineering Express

NOTE

Motor potential evoked by transcranial magnetic stimulation depends on the placement protocol of recording electrodes: a pilot study

To cite this article: Marco Antonio Cavalcanti Garcia *et al* 2020 *Biomed. Phys. Eng. Express* **6** 047003

Biomedical Physics & Engineering Express

RECEIVED
15 April 2020

REVISED
14 May 2020

ACCEPTED FOR PUBLICATION
20 May 2020

PUBLISHED
12 June 2020

NOTE

Motor potential evoked by transcranial magnetic stimulation depends on the placement protocol of recording electrodes: a pilot study

Marco Antonio Cavalcanti Garcia[1,2,3], **Victor Hugo Souza**[3,4], **Jordania Lindolfo-Almas**[1], **Renan Hiroshi Matsuda**[3] and **Anaelli Aparecida Nogueira-Campos**[2]

[1] Programa de Pós-Graduação em Ciências da Reabilitação e Desempenho Físico-Funcional, Faculdade de Fisioterapia, Universidade Federal de Juiz de Fora, Juiz de Fora, Brazil

[2] Laboratório de Neurofisiologia Cognitiva, Departamento de Fisiologia, Instituto de Ciências Biológicas, Universidade Federal de Juiz de Fora, Juiz de Fora, Brazil

[3] Laboratório de Biomagnetismo, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil

[4] Department of Neuroscience and Biomedical Engineering, Aalto University School of Science, Espoo, Finland

E-mail: marco.garcia@ufjf.edu.br

Keywords: motor evoked potential, surface electromyography, corticospinal excitability, transcranial magnetic stimulation, TMS, MEP

Abstract

Objective: There seems to be no consensus in the literature regarding the protocol of surface electromyography (sEMG) electrode placement for recording motor evoked potentials (MEP) in transcranial magnetic stimulation (TMS) applications. Thus, the aim of this study was to investigate the effect on the MEP amplitude bytwo different protocols for electrode placement. Methods: sEMG electrodes were placed on three upper arm muscles (*biceps brachii*, *flexor carpi radialis,* and *flexor pollicis brevis*) of six right-handed subjects following two different protocols (1 and 2), which varied according to the interelectrode distance and location relative to the muscle. TMS pulses were applied to the *hotspot* of *biceps brachii*, while sEMGwas recorded from the two protocols and for each muscle simultaneously. Main Results: Greater MEP amplitudes were obtained for Protocol 1 compared to Protocol 2 ($P < 0.05$). Significance: Different electrode placement protocols may result in distinct MEP amplitudes, which should be taken into account when adjusting the intensity on single and repetitive TMS sessions.

1. Introduction

The amplitude of the motor evoked potential (MEP) recorded with surface electromyography (sEMG) is the most common parameter used for determining the intensity of transcranial magnetic stimulation (TMS) in neurophysiological and treatment approaches. MEP amplitude critically depends on the electrode shape, size, placement relative to the muscle fibers, and on the muscle properties such as fiber architecture and size [1–3]. Although there are some recommendations regarding the use of sEMG for many clinical applications [2, 4–6], to our best knowledge, there is no consensus concerning the protocol of electrode placement for TMS applications. This methodological issue was recently addressed by Garcia *et al* [7], who reinforced the need for standardization on the electrode placement for recording MEPs. Garcia *et al* [7] suggested that the electrodes should be placed over the neuromuscular junction and a bony prominence for recording MEPs with maximal amplitudes. In turn, the Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles (SENIAM) recommendations [2] for surface electrodes placement was the first proposal for the standardization of sensor location with the aim, among other objectives, of minimizing the crosstalk between electrodes by adjusting the interelectrode distance depending on the muscle size. As far as we know, there is no previous data on how conventional electrode placement protocols affect the MEP amplitude. If MEP amplitudes vary depending on the placement protocols, the outcome of research and clinical TMS studies might lead to conflicting results. Thus, the present pilot study investigated the

Table 1. Descriptive data from each participant.

Participant	Age	Gender	rMT_{RH}	rMT_{LH}
1	26	F	41	42
2	49	M	58	60
3	37	M	53	44
4	25	F	56	60
5	18	F	45	47
6	26	F	45	42

Age (years) ; Gender: Female [F] and Male [M]; Resting Motor Thresholds (rMT) for right (RH—non-dominant) and left (LH–dominant) cerebral hemispheres obtained from the minimum TMS intensity to elicit MEPs with at least 100 μV of peak-to-peak amplitude.

effects of the protocols proposed by SENIAM [2] and Garcia *et al* [7] on the MEP amplitude recorded from three upper limb muscles commonly studied with TMS.

2. Methods

2.1. Participants

Six participants, all free of neurological and motor disorders (4 females; 18–49 years old), participated in this study. They all self-reported as right handed for daily living tasks. This study was approved by the local ethical committee (CAEE: 01158218.0.0000.5147) and followed the Declaration of Helsinki. Informed consent was obtained from all participants prior to the experimental session. The information of each participant is presented in table 1.

2.2. Surface EMG

2.2.1. Montages

Surface EMG signals were recorded from the *biceps brachii* (BB), *flexor carpi radialis* (FCR), and *flexor pollicis brevis* (FPB) of the right and left upper limbs of each subject using an EMG signal amplifier (EMG System do Brasil Ltda, São José dos Campos, Brazil; model: 410C; gain: 2000, sampling frequency: 3.5 kHz per channel; filter: band-pass 4th order Butterworth: 20–500 Hz; A/D conversor: 12 Bits). Surface electrodes (silver/silver chloride [Ag-AgCl]; 1 cm diameter; 2223 BRQ-3M) were placed on the three muscles according to two different recommendations. In Protocol 1 [7], electrodes were placed in a pseudo-monopolar montage with one electrode over the muscle's innervation zone and the other over the nearest bony prominence. The muscles' innervation zones were located based on an atlas [8], and confirmed using electrical stimulation (Meridian Energy Acupuncture Pen, Guangzhou Fabulous BYL Beauty Instrument Co., Ltd, China). In Protocol 2, a pair of electrodes were placed on the muscle belly with an interelectrode distance of 1 or 2 cm, depending on the muscle, according to the SENIAM [2]. Figure 1 provides a schematic view of the adopted electrode placement protocols. The reference electrode was placed over the cervical prominence C7. The skin was shaved and cleaned with neutral soap and alcohol before the placement of the electrodes.

2.3. TMS

Shoulder and elbow joints were kept on neutral and flexed (~90°) positions, respectively, and forearms resting on neutral position on a pillow during the whole experimental session. MEPs were recorded from both protocols (1 and 2) simultaneously for each muscle. Between thirty and forty TMS pulses (Magstin 200^2, figure-of-eight coil) were applied for 4 min to the BB muscle *hotspot* with an intensity of 120% of the resting motor threshold (rMT) in pseudo-randomized intervals of 5–10 s. The BB muscle was chosen as reference since it has the highest rMT among the three studied muscles [9, 10]. The rMT was defined as the minimum intensity needed to evoke MEPs larger than 100 μV peak-to-peak amplitude [11, 12] in at least five out of ten pulses. A cap containing a 1- cm^2 spaced grid positioned over the participant's skull was used to guide the coil placement during the whole recording session. TMS pulses were applied by the same experimenter throughout the sessions. Stimulation on BB muscle *hotspot* consistently evoked MEPs from the three monitored muscles simultaneously. The participants were vision-deprived during the sEMG recording.

2.4. Statistical analysis

The sEMG signals were processed and analyzed using the Signal Hunter [13] software (MATLAB version 8.1 R2013a, Mathworks Inc., Natick, MA, USA). Peak-to-peak amplitude was extracted from the MEPs. A linear mixed model was applied to assess the effects of protocol type, muscles, and limb sides on the natural logarithm of the MEP amplitude. The linear mixed model had a fixed (interaction between protocols, muscles, and limb sides) and a random structure (correlated random intercepts and slopes for protocols and muscles). The random structure was selected based on a sequential testing of hierarchical modelling with each model fit using likelihood ratio tests. The selected model was recomputed using restricted maximum likelihood estimation and p-values estimated using Satterthwaite approximations in a Type III Analysis of Variance. Post-hoc comparisons were performed with estimated marginal means with false discovery rate correction for p-values. The residuals of the model were inspected for deviations from normality and a scale-location plot analyzed to check the assumption of equal variance (homoscedasticity). The analysis was performed in scripts written in R version 3.6 (R Core Team, Vienna, Austria). The level of significance was set at 0.05.

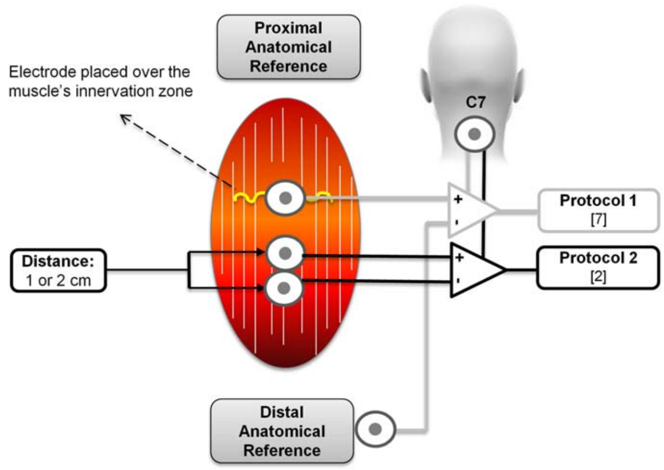

Figure 1. Schematic representation of the electrodes positioning according to the investigated protocols 1 [2] and 2 [7]. The proximal and distal anatomical references, as well as the muscles' innervation zones, were taken as the anatomical landmarks for the placement of the electrodes.

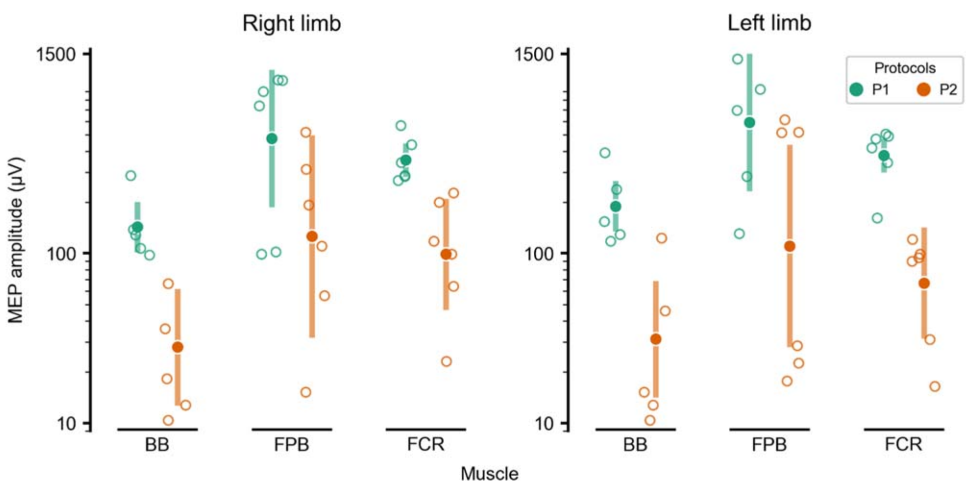

Figure 2. Model predictions and 95% confidence intervals of the MEP amplitudes obtained from the two electrode placement protocols (P1 and P2) in the muscles *flexor pollicis brevis* (FPB), *flexor carpi radialis* (FCR), and *biceps brachii* (BB) on the right and left limbs. The open circles represent the median MEP amplitude for each subject in each condition. The MEP amplitude axes in both charts are in logarithmic scale.

3. Results

The MEP amplitude for each protocol, muscle, and limb side is presented in figure 2. The protocols for electrode placement resulted in different MEP amplitudes depending on the target muscle (protocol × muscle; $F_{2,\ 2213.2} = 5.61$; $P < 0.01$). Overall, Protocol 1 generated higher MEP amplitudes than Protocol 2 (protocol; $F_{1,\ 5.0} = 32.00$; $P < 0.01$). On the FPB muscle, Protocol 1 resulted in MEP amplitudes about 3.8 and 5.3 times higher than in Protocol 2 on the right and left limbs, respectively ($P < 0.01$). For the FCR muscle, Protocol 1 showed MEP amplitudes about 3.6 and 5.6 times higher than in Protocol 2 for the right and left limbs, respectively ($P < 0.05$). Finally, for the BB muscle, Protocol 1 recorded MEP amplitudes 5.1 and 6.1 times higher than Protocol 2 ($P < 0.01$) on the right and left limbs, respectively (figure 2).

4. Discussion

The temporal and spectral contents of the sEMG signal strongly depend on the selected protocol of surface electrodes positioning [1, 3]. Nonetheless, the standards in electrode placement seem to be disregarded by several TMS studies [14–18]. Therefore, in this study, we evaluated two electrode placement protocols: Protocol 1 as suggested by Garcia *et al* [7] and Protocol 2 following the SENIAM recommendations [2]. Our results strongly suggested that the MEP amplitude depends on the electrode placement protocol, which may have a direct impact on comparisons across studies and on TMS treatment outcomes.

Protocol 1 resulted in 3.5 to 6.1 times higher MEP amplitudes compared to Protocol 2 for the three muscles investigated, which is most likely explained by the distinct operating principles of each protocol. Protocol

1 records the MEP in a monopolar configuration over the neuromuscular junctions and would result in a higher probability of action potentials coherent summation when reaching the muscle fibers [7]. The coherent summation leads to MEPs with greater amplitude. It is interesting to note that the adoption of this type of protocol was recently advocated by Stålberg *et al* [19] in neurography evaluations, i.e., when peripheral electrical nervous stimuli are applied. According to the authors, the placement of an electrode on the neuromuscular junction offered more robust latency estimates, which would also be another advantage for this type of protocol in TMS applications. On the other hand, Protocol 2 was designed to reduce the level of crosstalk during signal acquisition using interelectrode distances between 1–2 cm, depending on the muscle. The crosstalk from neighbor muscles contaminates the MEPs recorded in the forearm with conventional EMG montages [20, 21]. In this case, the use of high-density sEMG might provide additional insights for the electrode placement based on the MEP spatial distribution over the entire muscle extent [22]. Even so, the relatively small distance between electrodes in Protocol 2 may offer a reduced volume conductor when recording MEPs even from small muscle, such as the FPB, reducing the total evoked myoelectric activity when compared to Protocol 1.

The MEP amplitude is routinely adopted as a parameter to evaluate the integrity of the corticospinal pathway and in the interpretation of the process of integration and processing of cortical and subcortical areas in healthy and pathological subjects [10, 23]. Thus, the application of different protocols for the electrode placement in studies whose questions are similar could result in diverging outcomes, making it difficult to establish comparisons [24]. In addition, we should point out that the intensity of repetitive TMS (rTMS) is mainly defined relative to the MEP amplitude, and distinct electrode placement protocols may partially explain the divergences found in the literature regarding the efficacy of rTMS in the treatment of patients with similar diagnoses [25, 26], which is probably due to inappropriate dose delivery during the treatment.

We should note that the rMT in our study was adjusted to obtain 100-μV MEPs which is commonly used in multiple TMS studies [11, 12]. However, distinct adjustment of stimulation intensities may provide a different dependency of the MEP amplitude on the electrode placement.

Finally, our study was performed in a limited number of subjects and assessed only two electrode placement protocols. Nonetheless, the observed differences provide the first evidence that distinct protocols lead to large differences in MEP amplitude, and electrode placement should be carefully considered in brain stimulation studies and clinical applications.

5. Conclusion

Our study fosters the scientific community for the need of a standardized electrode placement on experiments recording MEPs, which seems to be significantly affected by the adopted protocol.

Acknowledgments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES)—Finance Code 001, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, Grant 2013/07699-0). This research was also supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq, [Grant number 426861/2016-7] to AANC. VHS is funded by the Jane & Aatos Erkko Foundation. The fundings had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

ORCID iDs

Marco Antonio Cavalcanti Garcia https://orcid.org/0000-0002-8225-6573
Victor Hugo Souza https://orcid.org/0000-0002-0254-4322
Jordania Lindolfo-Almas https://orcid.org/0000-0002-7369-0511
Renan Hiroshi Matsuda https://orcid.org/0000-0002-1927-4824
Anaelli Aparecida Nogueira-Campos https://orcid.org/0000-0001-8729-386X

References

[1] Lynn P A, Bettles N D, Hughes A D and Johnson S W 1978 Influence of electrode geometry on bipolar recordings of the surface electromyogram *Med. Biol. Eng. Comput.* **16** 651–60
[2] Hermens H J, Freriks B, Disselhorst-Klug C and Rau G 2000 Development of recommendations for SEMG sensors and sensor placement procedures *J. Electromyogr Kinesiol.* **10** 361–74
[3] Garcia M A C and Vieira T M M 2011 Surface electromyography: why, when and how to use it *Rev. Andal. Med. Deport.* **4** 17–28
[4] Groppa S *et al* 2012 A pratical guide to diagnostic transcranial magnetic stimulation: report of an IFCN committee *J. Clin. Neurophysiol.* **123** 858–82
[5] Legatt A D, Emerson R G, Epstein C M, MacDonald D B, Deletis V, Bravo R J and López J R 2016 ACNS guideline: transcranial electrical stimulation motor evoked potential monitoring *J. Clin. Neurophysiol.* **33** 42–50
[6] Tankisi H, Burke D, Cui L, de Carvalho M, Kuwabara S, Nandedkar S D, Rutkove S, Stålberg E, van Putten M J A M and Fuglsang-Frederiksen A 2020 Standards of instrumentation of EMG *J. Clin Neurophysiol.* **131** 243–58
[7] Garcia M A C, Souza V H and Vargas C D 2017 Can the recording of motor potentials evoked by transcranial magnetic stimulation be optimized? *Front Hum Neurosci.* **11** 413
[8] Barbero M, Merletti R and Rainoldi A 2012 *Atlas of Muscle Innervation Zones* (Milan: Springer)

[9] Vargas C D, Aballéa A, Rodrigues E C, Reilly K T, Mercier C, Petruzzo P, Dubernanrd J M and Sirigu A 2009 Re-emergence of hand-muscle representations in human motor cortex after hand allograft *Proc. Natl. Acad. Sci. U S A.* **106** 7197–202

[10] Garcia M A C, Catunda J M Y, Souza M N, Fontana A P, Sperandei S and Vargas C D 2016 Is the frequency in somatosensory electrical stimulation the key parameter in modulating the corticospinal excitability of healthy volunteers and stroke patients with spasticity? *Neural Plast.* **2016** 3034963

[11] Nogueira-Campos A A, de Oliveira L A S, Della-Maggiore V, Esteves P O, Rodrigues E C and Vargas C D 2014 Corticospinal excitability preceding the grasping of emotion-laden stimuli *PLoS One* **9** e94824

[12] Borgomaneri S, Vitale F, Gazzola V and Avenanti A 2015 Seeing feaful body language rapidly freezes the observer's motor cortex *Cortex.* **65** 232–45

[13] Souza V H, Peres A, Zacharias L and Baffa O 2015 SignalHunter: Software for electrophysiological data analysis and visualization (Version v1.0.0) (https://doi.org/10.5281/zenodo.1326307)

[14] Golaszewski S, Schwenker K, Bergmann J, Brigo F, Christova M, Trinka E and Nardone R 2016 Abnormal short-latency synaptic plasticity in the motor cortex of subjects with Becker muscular dystrophy: a rTMS study *Neurosci. Lett.* **610** 218–22

[15] Pedapati E V, Gilbert D L, Erickson C A, Horn P S, Shaffer R C, Wink L K, Laue C S and Wu S W 2016 Abnormal cortical plasticity in youth with autism spectrum disorder: a transcranial magnetic stimulation case-control pilot study *J. Child Adolesc. Psychopharmacol.* **26** 625–31

[16] Tang Z-, Xuan C-, Li X, Dou Z-, Lan Y- and Wen H- 2019 Effect of different pulse numbers of transcranial magnetic stimulation on motor cortex excitability: single-blind, randomized cross-over design *CNS Neurosci. Ther.* **25** 1277–81

[17] Hannah R, Rocchi L, Tremblay S, Wilson E and Rothwell J C 2020 Pulse width biases the balance of excitation and inhibition recruited by transcranial stimulation *Brain Stimul.* **13** 536–8

[18] Muellbacher W, Ziemann U, Boroojerdi B, Cohen L and Halltett M 2001 Role of the human motor cortex in rapid motor learning *Exp. Brain Res.* **136** 431–8

[19] Stålberg E *et al* 2019 Standards for quantification of EMG and neurography *J. Clin. Neurophysiol.* **130** 1688–729

[20] Neva J L, Gallina A, Peters S, Garland S J and Boyd L A 2017 Differentiation of motor evoked potentials elicited from multiple forearm muscles: an investigation with high-density surface electromyography *Brain Res.* **1676** 91–9

[21] Gallina A, Peters S, Jason L, Neva J L, Boyd L A and Garland S J 2017 Selectivity of conventional electrodes for recording motor evoked potentials: an investigation with high-density surface electromyography *Muscle Nerve.* **55** 828–34

[22] Souza V H, Vieira T M, Peres A S C, Garcia M A C, Vargas C D and Baffa O 2018 Effect of TMS coil orientation on the spatial distribution of motor evoked potentials in an intrinsic hand muscle *Biomed. Tech. (Berl).* **63** 635–45

[23] Peres A S C *et al* 2018 Can somatosensory electrical stimulation relieve spasticity in post-stroke patients? A TMS pilot study *Biomed. Tech. (Berl)* **63** 501–6

[24] Catroflorio T, Farina D, Bottin A, Piancino M G, Bracco P and Merletti R 2005 Surface EMG of jaw elevator muscles: effect of electrode location and inter-electrode distance *J. Oral. Rehabil.* **32** 411–7

[25] Rollnik J D, Huber T J, Mogk H, Siggelkow S, Kropp S, Dengler R, Emrich H M and Schneider U 2000 High frequency repetitive magnetic stimulation (rTMS) of the dorsolateral prefontral cortex in schizophrenic patients *Neuroreport.* **11** 4013–5

[26] Saba G, Verdon C M, Kalalou K, Rocamora J F, Dumontier G, Benadhira R, Stamatiadis L, Vicaut E, Lipski H and Januel D 2006 Transcranial magnetic stimulation in the treatment of schizophrenic symptoms: a double blind sham controlled study *J. Psychiatr. Res.* **40** 147–52