

Supplementary Document for *Correlating active
and resting motor thresholds for transcranial
magnetic stimulation through a matching model*

Table S1: Selected studies including both AMT and RMT measurements from the first dorsal interosseous muscle.

| Studies | Sample Size (F:M) | Device | Coil Type | Pulse Shape | Stimulated Hemisphere (Target Muscle) | % MVC | Hand | Dominance | Region |
|-----------------------|----------------------|--|-----------------|-------------------------|--|----------|--------------|-----------|-----------|
| Di Lazzaro et al. [1] | 7 F:3 M | Magstim 200 stimulator | Figure-of-eight | Monophasic | Left/Right M1 (FDI) | 20 % | NG | | Italy |
| Guerra et al. [2] | 6 F:12 M | Magstim 200 stimulator | Figure-of-eight | Monophasic | Left M1 (FDI) | 20 % | NG | | Italy |
| Hamada et al. [3] | 29 F:35 M | Magstim Super Rapid stimulator and Magstim 200 ² stimulator | Figure-of-eight | Biphasic and Monophasic | Left M1 (FDI) | 10 % | NG | | UK |
| Hand et al. [4] | 8 F:25 M | Two Magstim 200 ² stimulators with a Bistim unit | Figure-of-eight | Monophasic | Left M1 (FDI) | 10 % | NG | | Australia |
| Hand et al. [5] | 7 F:21 M | Two Magstim 200 ² stimulators with a Bistim unit | Figure-of-eight | Monophasic | Left M1 (FDI) | 10 % | NG | | Australia |
| Opie et al. [6] | 2 F:9 M | Two Magstim 200 stimulators with a Bistim unit | Figure-of-eight | Monophasic | Left M1 (FDI) | 5 – 10 % | Right-handed | | Australia |
| Sasaki et al. [7] | 10 F:21 M | Magstim Super Rapid stimulator and Magstim 200 ² stimulator | Figure-of-eight | Biphasic and Monophasic | Left M1 (FDI) | 10 % | Right-handed | | Japan |
| Wiethoff et al. [8] | 33 F:20 M | Magstim 200 ² stimulator | Figure-of-eight | Monophasic | Left M1 (FDI) | 10 % | Right-handed | | UK |
| Total Studies = 8; | | Total Subjects = 248 (102 F:146 M); | | | | | | | |

Note: (a) M1: the primary motor cortex, FDI: the first dorsal interosseous muscle; (b) Hemisphere: the target muscle is contralateral to the hemisphere being stimulated; (c) % MVC: the percentage of maximum voluntary contraction during AMT; (d) NG: not given; (e) Hamada et al. [3] provided unpublished data of MT measurements including extra 8 (5 F:3 F) subjects.

The present study follows the motor threshold measurement guidelines outlined by the International Federation of Clinical Neurophysiology. According to these guidelines, AMT is defined as the lowest stimulus strength that can produce MEPs of at least 200 μ V in about half of the trials during voluntary contraction of the target muscle at a certain percentage of the maximum voluntary contraction (MVC) and RMT is the lowest stimulus strength that can produce MEPs of at least 50 μ V in half of the stimuli in a relaxed target muscle [9]. In this study, the first dorsal interosseous (FDI) muscle was chosen as the target muscle, as it has been extensively used in previous studies that have measured both AMT and RMT [1, 2, 3, 4, 5, 6, 7, 8].

As listed in Table S1, this database has 248 subjects collected from eight different studies, which contains a number of 535 pairs of AMT and RMT, 1169 AMTs, and

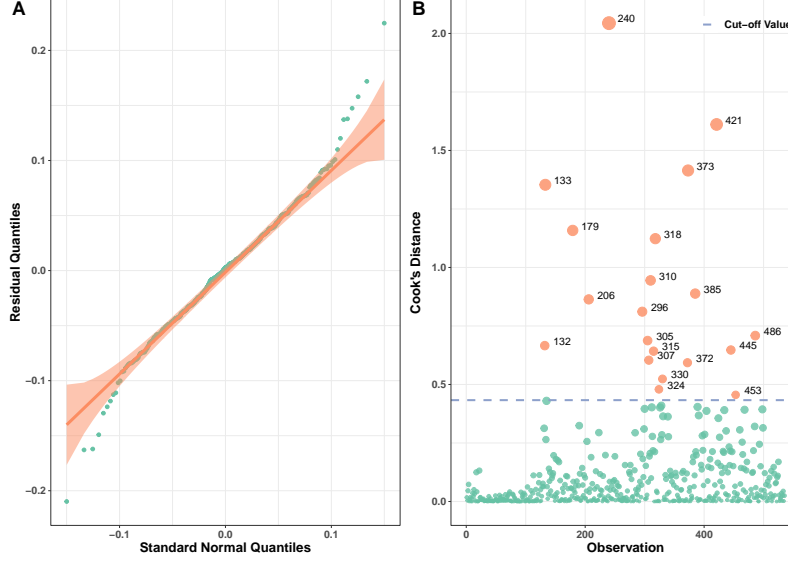


Figure S1: Illustration of the distribution of residuals and their corresponding Cook's Distance. (A) shows the standard quantile-quantile plot for the residuals of the calibrated model; (B) shows their Cook's distance and influential observations. The cut-off value is 4.5 times the residual mean, which is 0.433, in this study.

636 RMTs in total, and contains four TMS devices coming from Magstim and reports their specifications in detail as well. Moreover, this dataset is very unbalanced in terms of PULSE SHAPE and STIMULATED HEMISPHERE. The calibrated model with the original database shows that the model residual distribution ($\epsilon_{ijk} \sim \mathcal{N}(0, 3.5 \cdot 10^{-3})$) violates the assumptions of homogeneity of variance ($F(247, 287) = 1.78, p = 1.25 \cdot 10^{-6}$, Levene's test) but the assumption of normality ($P = 27.757, p = 0.184$, Chi-square normality test). To ensure the residual distribution assumptions of normality and homogeneity of variance, we calculated Cook's Distance for each residual and identified those observations that have a Cook's Distance greater than 4.5 times the residual mean (i.e., the cut-off value) as outliers (shown in Figure S1). Therefore, there are in total 20 observations identified as outliers in this database. In conclusion, the amended database for calibration has in total 515 observations and 237 subjects coming from eight studies.

Moreover, we applied mixed-effect models for analysing AMT and RMT respec-

tively by including Region (categorical), AGE (continuous), SEX (categorical), STIMULATED HEMISPHERE (categorical), and PULSE SHAPE (monophasic vs. biphasic, categorical) as fixed-effect variables. Similarly, we also considered two random-effect sources: STUDY and SUBJECT nested within STUDY, which is termed SUBJECT(STUDY) for AMT and RMT analysis. Note that AMT and RMT are all log-transformed. The model for AMT demonstrates a significant dependence of the AMT on the PULSE SHAPE ($F(1, 947.89) = 187.4034, p < 2 \cdot 10^{-16}$) and AGE ($F(1, 185.17) = 4.1357, p = 0.04341$), while the model for RMT shows a significant dependence on PULSE SHAPE ($F(1, 396.48) = 193.7927, p < 2 \cdot 10^{-16}$) but not AGE. The other fixed-effect factors, e.g., SEX, REGION, STIMULATED HEMISPHERE, did not show significant effects for both AMT and RMT models.

References

- [1] Di Lazzaro V, Dileone M, Pilato F, Capone F, Musumeci G, Ranieri F, et al. Modulation of motor cortex neuronal networks by rTMS: comparison of local and remote effects of six different protocols of stimulation. *Journal of neurophysiology* 2011; 105:2150–2156.
- [2] Guerra A, Suppa A, Asci F, De Marco G, D’Onofrio V, Bologna M, et al. LTD-like plasticity of the human primary motor cortex can be reversed by γ -tACS. *Brain Stimulation* 2019; 12:1490–1499.
- [3] Hamada M, Murase N, Hasan A, Balaratnam M, and Rothwell JC. The role of interneuron networks in driving human motor cortical plasticity. *Cerebral cortex* 2013; 23:1593–1605.
- [4] Hand BJ, Opie GM, Sidhu SK, and Semmler JG. Motor cortex plasticity and visuo-motor skill learning in upper and lower limbs of endurance-trained cyclists. *European Journal of Applied Physiology* 2022; 122:169–184.
- [5] Hand BJ, Opie GM, Sidhu SK, and Semmler JG. Motor cortex plasticity is greater in endurance-trained cyclists following acute exercise. *Journal of Applied Physiology* 2022; 133:932–944.
- [6] Opie GM, Catcheside PG, Usmani ZA, Ridding MC, and Semmler JG. Motor cortex plasticity induced by theta burst stimulation is impaired in patients with obstructive sleep apnoea. *European Journal of Neuroscience* 2013; 37:1844–1852.
- [7] Sasaki T, Kodama S, Togashi N, Shirota Y, Sugiyama Y, Tokushige Si, et al. The intensity of continuous theta burst stimulation, but not the waveform used to elicit motor evoked potentials, influences its outcome in the human motor cortex. *Brain stimulation* 2018; 11:400–410.
- [8] Wiethoff S, Hamada M, and Rothwell JC. Variability in response to transcranial direct current stimulation of the motor cortex. *Brain stimulation* 2014; 7:468–475.

- [9] Rossini PM, Burke D, Chen R, Cohen L, Daskalakis Z, Di Iorio R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an IFCN Committee. *Clinical neurophysiology* 2015; 126:1071–1107.