Journal of Neuroscience Methods 405 (2024) 110107

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Accelerometry as a tool for measuring the effects of transcranial magnetic stimulation

Gautier Hamoline [a,*,1], Elise E. Van Caenegem [a], Baptiste M. Waltzing [a], Pierre Vassiliadis [a,b], Gerard Derosiere [a,c], Julie Duque [a], Robert M. Hardwick [a]

[a] Institute of Neurosciences, UC Louvain, Avenue Mounier 54, Bruxelles 1200, Belgium
[b] Defitech Chair of Clinical Neuroengineering, Neuro-X Institute (INX) and Brain Mind Institute (BMI), École Polytechnique Fédérale de Lausanne (EPFL), Geneva 1202, Switzerland
[c] Université Claude Bernard Lyon 1, INSERM, Centre de Recherche en Neurosciences de Lyon U1028 UMR5292, IMPACT Team, Lyon, France

ARTICLE INFO

Keywords:
Transcranial magnetic stimulation
Electromyography
Accelerometry

ABSTRACT

Objective: We predicted that accelerometry would be a viable alternative to electromyography (EMG) for assessing fundamental Transcranial Magnetic Stimulation (TMS) measurements (e.g. Resting Motor Threshold (RMT), recruitment curves, latencies).
New Method: 21 participants were tested. TMS evoked responses were recorded with EMG on the First Dorsal Interosseus muscle and an accelerometer on the index fingertip. TMS was used to determine the (EMG-defined) RMT, then delivered at a range of intensities allowing determination of both the accelerometry-defined RMT and measurement of recruitment curves.
Results: RMT assessed by EMG was significantly lower than for accelerometry ($t(19)=-3.84$, $p<.001$, mean±SD EMG = 41.1±5.28% MSO (maximum stimulator output), Jerk = 44.55±5.82% MSO), though RMTs calculated for each technique were highly correlated ($r(18)=.72$, $p<.001$). EMG/Accelerometery recruitment curves were strongly correlated ($r(14)=.98$, $p<.001$), and Bayesian model comparison indicated they were equivalent ($BF_{01}>9$). Latencies measured with EMG were lower and more consistent than those identified using accelerometry ($\chi^2(1)=80.38$, $p<.001$, mean±SD EMG=27.01±4.58 ms, Jerk=48.4±15.33 ms).
Comparison with existing methods: EMG is used as standard by research groups that study motor control and neurophysiology, but accelerometry has not yet been considered as a potential tool to assess measurements such as the overall magnitude and latency of the evoked response.
Conclusions: While EMG provides more sensitive and reliable measurements of RMT and latency, accelerometry provides a reliable alternative to measure of the overall magnitude of TMS evoked responses.

1. Introduction

The effects of transcranial magnetic stimulation (TMS) have predominantly been studied on the primary motor cortex of the human brain (Hallett, 2000). Stimulating the motor cortical representation of a target muscle can lead to small movements of that muscle. Electrical activity in the muscle resulting from stimulation can be measured using electromyography (EMG), allowing the recording of the response as a 'Motor Evoked Potential' or MEP (Barker et al., 1985). The MEP has several characteristics, with the most frequently studied being its size, typically measured as the peak-to-peak amplitude in microvolts (μV). The dose-response relationship is used to derive several measurements, such as the Resting Motor Threshold' (RMT; the intensity of maximum stimulator output (MSO) that leads to a MEP of ≥50μV amplitude on ≥5/10 trials), and the 'recruitment curve' (created by taking the amplitude of the MEP response at different intensities of stimulation). A further characteristic of the MEP is the latency of the response, measured as the delay between the stimulation and the start of the MEP.

While electromyography (EMG) equipment is currently considered the gold standard for measuring responses to TMS, the technique faces several limitations. EMG has relatively high initial costs (apparatus, amplifiers) and ongoing costs (electrodes, electrode gel, cleaning

* Correspondence to: Avenue Mounier, 54 Claude-Bernard (2ème étage, bureau 0431), Woluwe-Saint-Lambert 1200, Belgique.
E-mail address: gautier.hamoline@uclouvain.be (G. Hamoline).
[1] https://uclouvain.be/fr/instituts-recherche/ions

https://doi.org/10.1016/j.jneumeth.2024.110107
Received 8 May 2023; Received in revised form 26 February 2024; Accepted 4 March 2024
Available online 8 March 2024

alcohol, etc) that make it relatively expensive (Ambrosini et al., 2018). Knowledge of the anatomy and physiology of the targeted muscle is required to find the correct area to position the electrodes (Micera et al., 2010). Additionally, several steps are required to optimize the EMG signal prior to data collection, including cleaning the skin, shaving to remove hair if needed, applying electrode gel, and checking for a clear signal, which make EMG relatively time consuming (Peri et al., 2017). While EMG is used as standard by research groups that study motor control and neurophysiology, many laboratories use EMG only to assess the RMT in order to determine the 'dose' at which to apply repetitive TMS over non-motor areas (typically 110–120% of RMT – see for examples Cantello et al., 2007; Hoogendam et al., 2010; Ikeguchi et al., 2005); in these situations, the monetary and time costs associated with EMG make it less desirable. Consequently, many research groups assess the RMT using visual inspection; an experimenter observes the target muscle and determines whether activity was elicited in response to TMS (Balslev et al., 2007; Pridmore et al., 1998), with RMT being identified as the minimum intensity of maximal stimulator output at which at least 5/10 stimuli result in a visually detectable contraction of the target muscle. Unfortunately, visual inspection is highly subjective (Pridmore, 1998), and does not provide a precise measure of the magnitude of the response to TMS. This is a concern as over-estimating the RMT could lead to experimenters delivering intensities of stimulation that exceed the safety guidelines for TMS protocols (Rossi et al., 2009). Developing alternative approaches that are cheaper and faster to apply than EMG, but also provide more accurate quantification of responses than visual inspection, could therefore be of benefit to researchers using TMS.

Accelerometry provides a potential approach to address the issues identified when using EMG or visual inspection to assess the response to TMS. Specifically, it is relatively cheap to implement and has lower ongoing costs compared to EMG, while also allowing researchers to quantify the response to TMS in a more objective manner than visual inspection. Several groups have previously used accelerometry to assess how the direction and magnitudes of movements evoked by TMS changes in response to training (Classen et al., 1998; Duque et al., 2008; Mawase et al., 2017). However, accelerometry has not yet been considered as a potential tool to assess measurements such as the resting motor threshold, the overall magnitude, and latency of the evoked response.

The present study therefore examined whether accelerometry could provide a potential alternative to the use of EMG when measuring responses to TMS. To compare accelerometry to the current 'gold-standard', we assessed several standard measures of the TMS evoked response (i.e. RMT, recruitment curve, response latency) using both EMG and accelerometry.

2. Materials and methods

2.1. Participants

In the present study we collected TMS data from 22 subjects. One participant withdrew from the study, bringing the total to 21 subjects (age mean±SEM 24.40±0.59, range 20–31, 13 females, 8 males, 19 right-handed, 2 left-handed). All subjects gave written informed consent, and the experiment was approved by the Ethics Committee Saint-Luc Hospital, UCLouvain.

2.2. Transcranial magnetic stimulation

TMS was delivered using a monophasic Magstim 200^2 with a figure-of-eight coil (2 x Ø70 mm). A tightly fitting electroencephalography cap was worn on the head to help to mark scalp locations for the application of the TMS. The nasion-inion line and the interaural line were used as the reference for the stimulus sites (Mathias et al., 2014).

2.3. Electromyography

EMG was used to measure MEPs from the First Dorsal Interosseus (FDI) muscle of the index finger of the dominant hand (Fig. 1A). Prior to electrode placement the skin was cleaned with an alcohol solution (and shaved if needed) to exfoliate dead skin cells and improve conductivity. A pair of Self-adhesive pre-gelled bipolar surface electrodes (Blue Sensor N, Ambu ®, Denmark) were then placed on the body and on the distal insertion of the skin over the muscle. A reference electrode was placed on the styloid process of the ulna. EMG was sampled at 2 kHz, and amplified with D360 8 Channel Patient Amplifier, Digitimer®, England. Recorded EMG signals were corrected for electrical interference using the reference noise method (Jiruska et al., 2009) and band-pass filtered with a 4th order Butterworth filter with a passband of 20–450 Hz offline before analysis.

2.4. Accelerometer recordings

An accelerometer (8791A250 K-Shear® Miniature Triaxial Accelerometer, Switzerland) was attached to the index finger using micropore adhesive tape (Fig. 1A). The accelerometer recorded movements in the x-y-z planes, allowing full reconstruction of the movement produced (4-Channel PiezoSmart® (TEDS) Power Supply/Signal Conditioner, Switzerland). The data were registered as the acceleration of the finger (m/s^2). Data were lowpass filtered using a 20 Hz 4th order Butterworth filter offline before analysis.

2.5. Protocol design

Participants sat on a chair with the palmar side of the dominant hand resting face down on the table. The participant had the opportunity to adjust their position, including the position and/or height of the table and/or chair, and the opportunity to use pillows to find the best position to be comfortable and relax during all the testing periods.

We first identified the corticomotor area corresponding to the index finger on the contralateral hemisphere to the dominant hand, identifying the 'motor hotspot' region that induced responses in FDI. We then assessed the RMT using EMG; the threshold was determined as the lowest intensity of TMS required to produce a response with an amplitude of at least 50μV in at least 5/10 trials (Chen et al., 1997). Finally, we assessed corticomotor recruitment curves, which measure the relationship between the intensity of stimulation applied via TMS and the magnitude of the evoked response, using EMG around the RMT ranging from –5% to +10% of MSO (e.g. the intensity '+1' refers to RMT+1% MSO). A total of 10 trials were collected at each intensity of stimulation. The order in which each intensity of stimulation was delivered was varied pseudorandomly for each participant. Later analyses also used this data to determine the RMT according to accelerometry.

2.6. Data processing

EMG and accelerometer data were captured using a Power1401–3A and Signal software, (both by Cambridge Electronic Design, England). Data were analysed using custom MATLAB scripts. EMG signals were analysed to identify the 'peak-to-peak' amplitude of the MEP response (measured as the difference between largest positive and negative peaks of the MEP). Accelerometer signals in the x,y, and z directions were combined using the cartesian equation ($absolute\ acceleration = \sqrt{x^2 + y^2 + z^2}$) to provide a single measurement of the overall acceleration of the sensor (providing a measurement that was sensitive to the possibility of any movement of the finger in response to TMS, which is equivalent to the measure used with visual inspection). The derivative of the acceleration was then calculated to provide a measurement of jerk (m/s^3), with the absolute peak jerk being identified as the main signal of interest. Jerk is useful when analyzing rapid or transient changes in

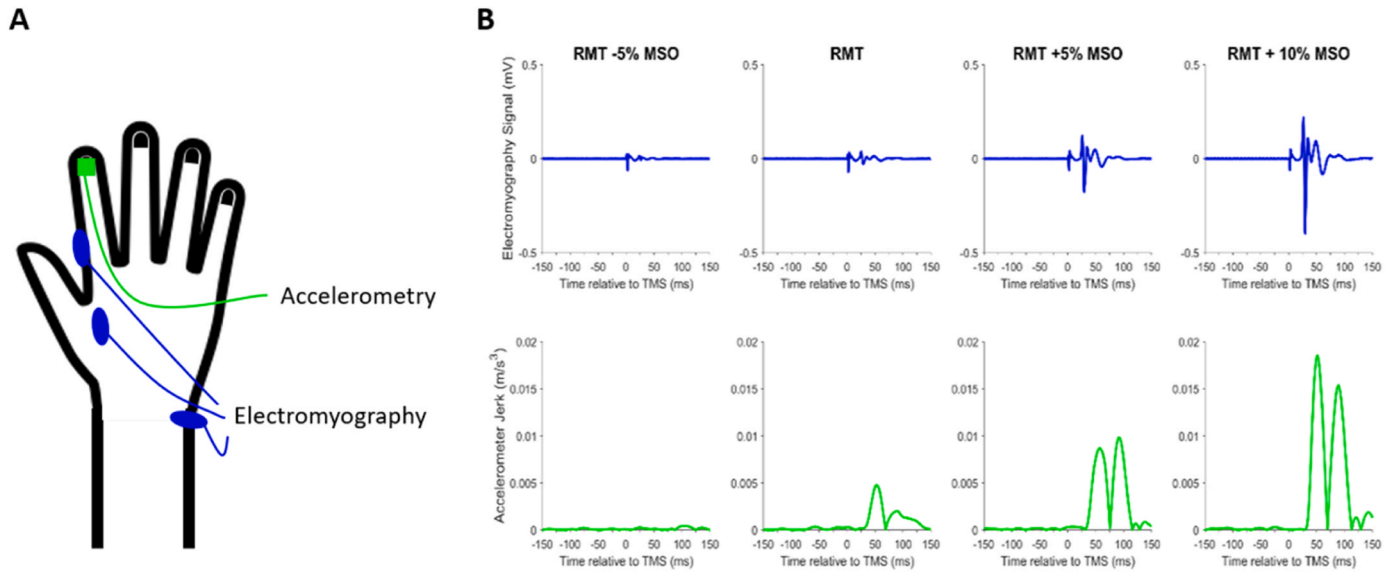

Fig. 1. Setup and Example data. A) schematic for the setup for electromyography and accelerometer measurements. Electrodes recorded signals from the first dorsal interosseus muscle of the dominant hand. An accelerometer was placed on the nail of the index finger of the hand. B) Example data for a single participant showing Electromyography data (upper row, blue) and Accelerometer data (lower rows, green - first peak in jerk corresponds to the initial acceleration/contraction phase, while the second peak represents the deceleration/ relaxation phase) at different intensities relative to the electromyography-defined Resting Motor Threshold (RMT). Each trace presents an average across 10 trials. MSO=Maximal Stimulator Output.

movement, and TMS-induced movements often involve quick and dynamic responses.

The processed accelerometry data was also used to identify the RMT as would be identified via accelerometry. This was determined as the intensity of MSO at which 5 out of 10 trials gave a peak jerk (m/s^3) outside of 95% confidence interval calculated in the 200 ms prior to TMS stimulation.

Latencies of the responses collected using EMG and accelerometry were calculated using the absolute hard threshold estimation (AHTE) algorithm (Šoda et al., 2020). Briefly, the time at which the TMS was delivered was identified, and the first 18 ms after stimulation was marked as a 'dropout zone' to account for the artefact from the stimulator discharge (see Šoda et al., 2020). The recorded data was then squared, and the latency was identified as the time between the delivery of the stimulus and the first time after the dropout zone at which the squared signal was >=10% of its maximum.

2.7. Statistical analyses

Data were analysed using repeated measures analysis of variance (ANOVA), t-tests, and correlations as appropriate (see below). Shapiro-Wilk tests examined the normality distribution of the different data, and if the assumption of normality was violated then the corresponding data were analysed using a non-parametric test (e.g Friedman's test).

The RMT as identified using EMG and accelerometry was examined using two approaches. First, a paired-samples t-test examined possible differences between the RMT as estimated using EMG and accelerometry, expressed as a percentage of MSO. A Pearson correlation test examined the extent to which the measurement of RMT provided with each technique were related.

Recruitment curves were assessed for each participant by calculating the mean average peak-to-peak MEP amplitudes and peak accelerometer jerk for each of the 16 intensities examined. The grand mean for each intensity across all subjects was then calculated. As measurements using EMG and Accelerometry are not directly comparable due to their differing units of measurement, data were rank-transformed to allow their combined analysis (Conover, 2012). Rank transformation was applied for each technique at intensities at and above the resting motor threshold (i.e. for each subject, the smallest mean response for EMG was ranked as 1, the largest 11, and the same process was conducted for the accelerometer data). These data were then analysed using a 2×11 repeated measures ANOVA with factors of measurement technique (EMG, accelerometry) and intensity (RMT to RMT+10). As well as traditional frequentist statistics, we also conducted Bayesian model comparison, allowing assessment of both differences and possible equivalences between the measurement techniques. Only data above the resting motor threshold was examined as stimulating at intensities below this level produced relatively few measurable responses, and thus any ranking of data at these intensities would primarily be based on noise. A Spearman's correlation coefficient test then assessed the relationship between raw peak-to-peak MEP amplitudes collected using EMG and peak accelerometry responses. Separate Spearman's correlation coefficient tests were also calculated to assess the relationship between EMG and accelerometry within each participant (using data from each of the 160 trials collected) to assess the variability of correlations between the subjects.

Mean average MEP latency and peak accelerometer latency values were calculated for each participant by averaging their response delays across the 10 trials taken at each intensity of stimulation. As a reliable MEP is required in order to assess response latencies, we examined response latencies at only the 6 highest intensities examined (RMT+5 to RMT+10). These data were then analysed using Friedman's test to compare the latencies identified by each method and possible effects of intensity on the measured response. Recent studies suggest that MEP latency remains stable even with varying intensities of TMS stimulation (Di Lazzaro et al., 2004; Kiers et al., 1993; Nielsen et al., 1995); therefore, to assess the variability of the responses provided by each technique, a final Friedman's test was used to compare the coefficient of variation from the latencies provided by EMG and accelerometry.

3. Results

3.1. Resting motor threshold

A first analysis compared the RMT as assessed using EMG (based on MEP amplitudes) and using accelerometry (based on peak jerk; Fig. 2A). A paired samples t-test indicated that the value for the RMT as estimated using EMG was significantly lower than the value estimated by

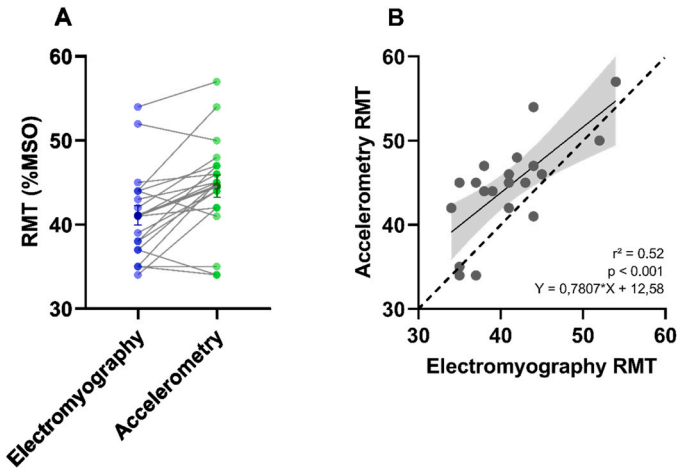

Fig. 2. Analysis of the Resting Motor Threshold (RMT). A) Resting motor threshold assessment with electromyography (blue circles) and with accelerometry (green circles). Each line presents data from an individual participant. Darker circles with error bars represent means for electromyography and accelerometry, error bars present ±1SEM. B) Correlation between the resting motor threshold assessed by electromyography and accelerometry, shaded area presents 95% confidence interval. MSO: Maximal Stimulator Output.

accelerometry (t(19)=-3.84, p<.001, mean ± SD EMG = 41.1+-5.28% MSO, Jerk = 44.55+-5.82% MSO). However, even though accelerometry generally over-estimated the RMT, the estimated value it provided was strongly correlated with the RMT as assessed using EMG (r(18)=.72, p<.001; Fig. 2B). Based on a linear regression model fit to these data, it is possible to take RMT values as determined using accelerometry (RMT_{ACC}) and predict the equivalent RMT value that would be determined using EMG (RMT_{EMG}) using the equation:

$$RMT_{EMG} = (RMT_{ACC} \times 0.667) + 11.26$$

.

3.2. Recruitment curves

The recruitment curve was examined based on results from EMG and accelerometry via different stimulator intensities (Fig. 3A). Analysis of ranked data from each technique identified a significant main effect of intensity ($F_{10,200}$ = 57.75, p <.001), but critically no main effect of technique ($F_{1,20}$ = 2.4e-14, p = 1.00), nor an interaction between technique and intensity ($F_{10,200}$ = 0.54, p = 0.86). Bayesian model comparison agreed with the frequentist analyses, indicating that the data were best explained by a model with the single factor of intensity

Table 1
Bayesian Model Comparison.

Models	P(M)	P(M| data)	BF_M	BF_{01}	error %
Intensity	0.200	0.907	38.876	1.000	
Technique + Intensity	0.200	0.093	0.408	9.791	1.285
Technique + Intensity + Technique*Intensity	0.200	6.832e-4	0.003	1327.054	1.249
Null model (incl. subject)	0.200	5.088e-95	2.035e-94	1.782e+94	0.350
Technique	0.200	5.088e-96	2.035e-95	1.782e+95	0.931

Note. All models include subject

Table 1: Model comparison for all models under consideration for the ranked repeated measures ANOVA on the recruitment curves. The 'Models' column shows the predictors in each model, the P(M) column the prior model probability, the P(M|data) column the posterior model probability, the BF_M column the posterior model odds, and the BF_{01} column the Bayes factors of all models compared to the best model (note $BF_{01\ signifies}$ these results are presented in relation to support for the null hypothesis i.e. that the best model is indeed the most appropriate for the data), the final column 'error %' is an estimate of the numerical error in the computation of the Bayes factor. All models are compared to the best model and are sorted from lowest Bayes factor to highest.

(see Table 1). In comparison to this model, models including a factor of technique, or an interaction between technique and intensity, showed evidence for the null hypothesis (all BF_{01}>9), suggesting equivalence between measurements taken with EMG and accelerometry.

Spearman's test identified a strong positive correlation between the two measurement techniques r(14)=0.98, p<.001; Fig. 3B). This data was based on group averages; we also conducted further analyses to examine the relationship between EMG and accelerometry measures at the level of individual participants. For each participant we calculated separate Spearman's correlation coefficient tests to assess the relationship between EMG and accelerometry. The average r value from these analyses indicated relatively strong correlations (mean ± SD = 0.57 ±0.18; full details presented in supplementary appendix 1).

3.3. Latency

Response latencies, and the variability of the measurements provided, were assessed using EMG and accelerometry. Friedman's test indicated that the latencies as estimated using EMG were significantly lower than the latencies estimated by accelerometry (χ^2(1)=80.38, p<.001, mean ± SD EMG = 27.01±4.58 ms, Jerk = 48.4±15.33 ms; Fig. 4A). There was no significant effect of stimulus intensity (χ^2(15)= 7.06, p=0.22; Fig. 4A). As previous work suggests MEP latencies are relatively stable through different intensities (Di Lazzaro et al., 2004; Kiers et al., 1993; Nielsen et al., 1995), to assess the variability of each

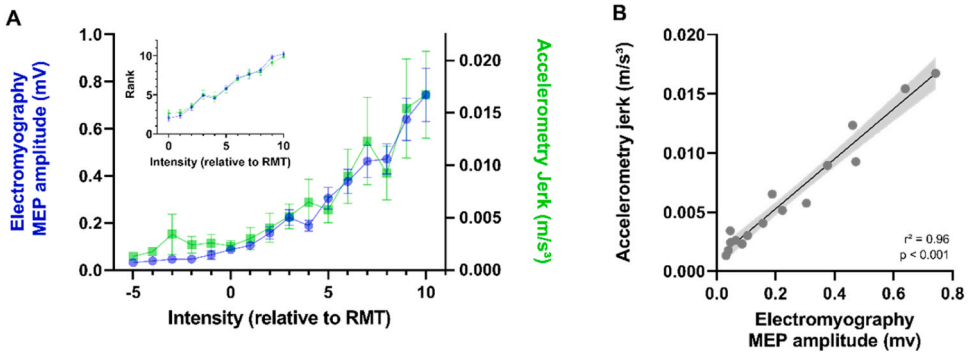

Fig. 3. Analysis of recruitment curves. A) Recruitment curve created with electromyography (blue circles, data corresponding to the left y-axis) in mV through intensities relative to the (EMG defined) resting motor threshold +/-x of maximal stimulator output, and recruitment curve created with accelerometry (green squares, data corresponding to the right y-axis) in jerk (m/s^3) through these intensities. Inset shows subset of data used in ranked analysis. All error bars present ±1SEM. B) Group-level correlation between the EMG measurement and accelerometry measurement. Shaded area presents 95% confidence interval.

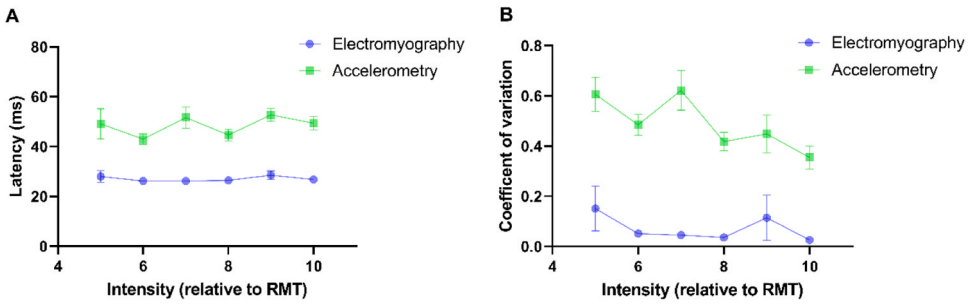

Fig. 4. Analysis of response latencies. A) Latency in ms assessed by electromyography (blue circles) and by accelerometry (green squares). Error bars expressed in SEM. B) the coefficient of variation as assessed by electromyography (blue circles) and by accelerometry (green squares). Error bars present ±1SEM.

measurement technique, a Friedman's test on the coefficient of variation of the latencies was calculated for the EMG and accelerometry data. The coefficient of variation for latencies estimated by accelerometry was found to be larger than latencies estimated by EMG ($\chi^2(1) = 87.29$, $p < .001$, mean±SD EMG = 0.16±0.14, Jerk = 0.31±0.14; Fig. 4B). There was no significant difference in the coefficient variation at different stimulus intensities ($\chi^2(5) = 9.7$, $p = .08$, Fig. 4B).

4. Discussion

Here we assessed the validity of accelerometry as a new tool to measure the effects of TMS. Results indicated strong correlations between the RMT and the recruitment curves assessed by EMG and accelerometry, suggesting accelerometry could be a useful tool for quantifying the magnitude of the response to TMS. However, the RMT and latency as estimated by accelerometry were both greater than those as assessed using EMG. These results corroborated our preliminary hypotheses that accelerometry could be a useful alternative to EMG, but indicate that the reliability of the technique is greater when obtaining multiple measurements, such as rTMS recruitment curves, and when the intensity of TMS is suitably high to elicit an unambiguous response.

We identified relatively strong correlations between the recruitment curves as assessed using EMG and accelerometry at both the group and individual levels. These results are consistent with previous TMS studies that have indicated that larger EMG responses are associated with greater accelerometer values (e.g. Duque et al., 2008; Mawase et al., 2017; Stefan et al., 2005), though to our knowledge the present study is the first to formally assess this effect and the associated dose-response relationship. Moreover, Bayesian model analysis indicated that EMG and accelerometry were equivalent in capturing the recruitment curve dose-response relationship to TMS. This result also indicates that accelerometry could be a useful tool in approaches such as cortical mapping, in which TMS is applied at intensities greater than the Resting Motor Threshold, as it can be used to reliably measure both the presence/absence and magnitude of evoked responses. As such, the strong correlation between EMG and accelerometry, and their equivalent ability to measure the amplitudes of TMS-evoked responses, is worthy of future investigation.

Although the assessment of RMT between EMG and accelerometry was highly correlated, accelerometry generally overestimated the threshold. This indicates that the transformation equation is necessary, even if it needs to be confirmed by further research. This could be explained by the character of the two measurement techniques. Electromyography measured the intrinsic contraction of the FDI muscle, while accelerometry measured the extrinsic acceleration of the finger. The latter must overcome inertia to move, and a small contraction may not produce enough force to induce a movement. To our knowledge, there is no scientific precedent for using accelerometry to establish the RMT; the closest link that can be made to previous research is measurements of the RMT through visual inspection. Results regarding the estimation of the resting motor threshold using EMG compared to visual inspection are somewhat inconsistent. Pridmore et al. (1998), showed an *underestimation* by visual inspection (mean ± SD= −3.2 ± 4.76) compared to the electromyography of the RMT, while Balslev et al. (2007) indicated that visual inspection *overestimated* the RMT by an average of 2% in comparison to EMG. By contrast, the present results indicate that measurement with accelerometry generally leads to an overestimation of the RMT compared to EMG (mean±SD= 3.6±4.2). As such, the RMT identified by accelerometry is generally overestimated, but could be useful as a more directly quantifiable approach to identifying the RMT compared to visual inspection. MEP latencies as estimated using EMG were significantly lower than the latencies estimated by accelerometry, and the latency measured with accelerometry was more variable. We attribute these differences, at least in part, to the nature of the signals being recorded by each technique. EMG is sensitive to electrical activity at the site of the muscle, the onset of which slightly proceeds the actual time at which a contraction/movement of the corresponding muscle occurs (Schmidt and Lee, 1999) By contrast, the accelerometer gives a measurement that results directly from movement, and as such is subject to several additional factors (e.g. inertia, frictional forces, time required to detect motion in relation to background noise, etc) that would not influence EMG activity. We further note that there is not a standard agreement upon way to measure the EMG latencies (techniques include 95%CI, onset of M-wave, AHTE, etc; Mamoei et al., 2020; Soda et al., 2020; Tataroglu et al., 2004). Here we chose the AHTE algorithm as it has been shown to provide good accuracy for EMG data and could readily be applied to accelerometry data. As such, we conclude that accelerometry does not provide a reliable measurement of MEP latencies, and that while alternative algorithms could be of interest, the present data indicate that the method of calculation used would be unlikely to change this result.

While the present findings indicate that accelerometry could feasibly be used as an alternative to EMG, these results face some limitations. The overestimation of the Resting Motor Threshold could be a key limitation, particularly in studies where this could be a safety concern. For example, studies using repetitive TMS would involve an increased level of risk if the RMT was over-estimated, as the 'dose' of stimulation is set relative to this intensity. However, researchers could reasonably use accelerometry to assess the RMT for single-pulse stimulation approaches, such as recording recruitment curves when TMS is applied on the primary motor cortex. Similarly, studies using cortical mapping approaches for deep-lying muscles, where the intensity of stimulation is set as high as 100% of MSO (Wassermann et al., 1992), could feasibly use accelerometry to measure motor responses. In this situation, care should be taken to ensure that the position of the accelerometer provides direct outcomes of the stimulation (for example, accelerometry on the hand will also record movements if the arm or shoulder move in response to stimulation).

Further limitations relate to the choice to use a single target muscle during the present study. The decision to focus on the First Dorsal Interosseus muscle is driven by the specific research question, as this is the most commonly used muscle when attempting the identify the

Resting Motor Threshold. The choice of the FDI therefore is based on its accessibility, relative simplicity, and well-understood physiological responses. Naturally, as the use of an accelerometer depends on the detection of motion, we anticipate it will be most appropriate when applied to the extremities of the lower or upper limbs, and unlikely to be relevant for applications such as detecting activity of core muscles.

The potential of accelerometry as a valuable tool in Transcranial Magnetic Stimulation (TMS) research is becoming increasingly evident. To advance this promising avenue, future research should aim to validate accelerometry on a broader scale. Expanding the scope of experiments and encompassing diverse TMS applications will provide a more comprehensive understanding of the reliability and versatility of accelerometry. This validation process should also address the challenge of overestimation of the resting motor threshold (RMT) when using accelerometry. It is essential to investigate and refine the linear transformation equation/model applied to correct for RMT overestimation. This correction is critical for ensuring the accuracy of TMS protocols and, ultimately, participant safety. Moreover, the potential to use accelerometry in cortical mapping studies is an intriguing prospect. Finally, accelerometry may provide a more objective alternative to visual inspection when attempting to identify the Resting Motor Threshold; future experiments may consider comparing measurements taken with visual inspection, accelerometry, and electromyography to elucidate the relationship between these three measurement techniques. Furthermore, at the time of writing, markerless, camera-based motion tracking approaches are becoming increasingly widespread, and may provide a further alternative approach for such measurements.

5. Conclusion

The present study compared measurements of the response to TMS using EMG and accelerometry. While EMG provides more sensitive measurements of RMT and response latency, accelerometry provides a reliable alternative to the measure of the 'peak' response to TMS. This makes accelerometry a promising tool for assessment of dose-response relationships to TMS, and could be of potential interest in approaches such as cortical mapping studies.

CRediT authorship contribution statement

Pierre Vassiliadis: Writing – review & editing, Methodology, Conceptualization. **Gerard Derosiere:** Writing – review & editing, Methodology, Conceptualization. **Julie Duque:** Writing – review & editing, Resources. **Robert M Hardwick:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Gautier Hamoline:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Elise E Van Caenegem:** Writing – review & editing, Methodology. **Baptiste M Waltzing:** Writing – review & editing.

Declaration of Competing Interest

None of the authors have potential conflicts of interest to be disclosed. Gautier Hamoline is supported by a PhD fellowship from the Faculty of Motricity Sciences, UCLouvain. Robert Hardwick is supported by grants from the UCLouvain Special Research Funds Seedfunds (grant FSR 1C21300057) and the Belgian Fund for Scientific Research (grants FNRS J.0084.21 and FNRS F.4523.23).

Data availability

Data will be made available on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jneumeth.2024.110107.

References

Ambrosini, E., Ferrante, S., van de Ruit, M., Biguzzi, S., Colombo, V., Monticone, M., Ferriero, G., Pedrocchi, A., Ferrigno, G., Grey, M.J., 2018. StimTrack: an open-source software for manual transcranial magnetic stimulation coil positioning. J. Neurosci. Methods 293, 97–104. https://doi.org/10.1016/j.jneumeth.2017.09.012.

Balslev, D., Braet, W., McAllister, C., Miall, R.C., 2007. Inter-individual variability in optimal current direction for transcranial magnetic stimulation of the motor cortex. J. Neurosci. Methods 162, 309–313. https://doi.org/10.1016/j.jneumeth.2007.01.021.

Barker, A.T., Jalinous, R., Freeston, I.L., 1985. Non-invasive magnetic stimulation of human motor cortex. Lancet Lond. Engl. 1, 1106–1107. https://doi.org/10.1016/s0140-6736(85)92413-4.

Cantello, R., Rossi, S., Varrasi, C., Ulivelli, M., Civardi, C., Bartalini, S., Vatti, G., Cincotta, M., Borgheresi, A., Zaccara, G., Quartarone, A., Crupi, D., Laganà, A., Inghilleri, M., Giallonardo, A.T., Berardelli, A., Pacifici, L., Ferreri, F., Tombini, M., Gilio, F., Quarato, P., Conte, A., Manganotti, P., Bongiovanni, L.G., Monaco, F., Ferrante, D., Rossini, P.M., 2007. Slow Repetitive TMS for Drug-resistant Epilepsy: clinical and EEG findings of a Placebo-controlled Trial. Epilepsia 48, 366–374. https://doi.org/10.1111/j.1528-1167.2006.00938.x.

Chen, R., Classen, J., Gerloff, C., Celnik, P., Wassermann, E.M., Hallett, M., Cohen, L.G., 1997. Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology 48, 1398–1403. https://doi.org/10.1212/wnl.48.5.1398.

Classen, J., Liepert, J., Wise, S.P., Hallett, M., Cohen, L.G., 1998. Rapid plasticity of human cortical movement representation induced by practice. J. Neurophysiol. 79, 1117–1123. https://doi.org/10.1152/jn.1998.79.2.1117.

Conover, W.J., 2012. The rank transformation—an easy and intuitive way to connect many nonparametric methods to their parametric counterparts for seamless teaching introductory statistics courses. WIREs Comput. Stat. 4, 432–438. https://doi.org/10.1002/wics.1216.

Di Lazzaro, V., Oliviero, A., Pilato, F., Saturno, E., Dileone, M., Mazzone, P., Insola, A., Tonali, P.A., Rothwell, J.C., 2004. The physiological basis of transcranial motor cortex stimulation in conscious humans. Clin. Neurophysiol. . J. Int. Fed. Clin. Neurophysiol. 115, 255–266. https://doi.org/10.1016/j.clinph.2003.10.009.

Duque, J., Mazzocchio, R., Stefan, K., Hummel, F., Olivier, E., Cohen, L.G., 2008. Memory formation in the motor cortex ipsilateral to a training hand. Cereb. Cortex 18, 1395–1406. https://doi.org/10.1093/cercor/bhm173.

Hallett, M., 2000. Transcranial magnetic stimulation and the human brain. Nature 406, 147–150. https://doi.org/10.1038/35018000.

Hoogendam, J.M., Ramakers, G.M.J., Di Lazzaro, V., 2010. Physiology of repetitive transcranial magnetic stimulation of the human brain. Brain Stimul. 3, 95–118. https://doi.org/10.1016/j.brs.2009.10.005.

Ikeguchi, M., Touge, T., Kaji, R., Deguchi, K., Sasaki, I., Tsukaguchi, M., Takeuchi, H., Kuriyama, S., 2005. Durable effect of very low-frequency repetitive transcranial magnetic stimulation for modulating cortico-spinal neuron excitability. Int. Congr. Ser. Unveiling Mystery Brain: Neurophysiol. Investig. Brain Funct. 1278, 272–275. https://doi.org/10.1016/j.ics.2004.11.189.

Jiruska, P., Cmejla, R., Powell, A.D., Chang, W.-C., Vreugdenhil, M., Jefferys, J.G.R., 2009. Reference noise method of removing powerline noise from recorded signals. J. Neurosci. Methods 184, 110–114. https://doi.org/10.1016/j.jneumeth.2009.07.003.

Kiers, L., Cros, D., Chiappa, K.H., Fang, J., 1993. Variability of motor potentials evoked by transcranial magnetic stimulation. Electroencephalogr. Clin. Neurophysiol. Potentials Sect. 89, 415–423. https://doi.org/10.1016/0168-5597(93)90115-6.

Mamoei, S., Hvid, L.G., Boye Jensen, H., Zijdewind, I., Stenager, E., Dalgas, U., 2020. Neurophysiological impairments in multiple sclerosis—Central and peripheral motor pathways. Acta Neurol. Scand. 142, 401–417. https://doi.org/10.1111/ane.13289.

Mathias, J.P., Barsi, G.I., van de Ruit, M., Grey, M.J., 2014. Rapid acquisition of the transcranial magnetic stimulation stimulus response curve. Brain Stimul. 7, 59–65. https://doi.org/10.1016/j.brs.2013.08.003.

Mawase, F., Uehara, S., Bastian, A.J., Celnik, P., 2017. Motor learning enhances use-dependent plasticity. J. Neurosci. 37, 2673–2685. https://doi.org/10.1523/JNEUROSCI.3303-16.2017.

Micera, S., Carpaneto, J., Raspopovic, S., 2010. Control of hand prostheses using peripheral information. IEEE Rev. Biomed. Eng. 3, 48–68. https://doi.org/10.1109/RBME.2010.2085429.

Nielsen, J., Petersen, N., Ballegaard, M., 1995. Latency of effects evoked by electrical and magnetic brain stimulation in lower limb motoneurones in man. J. Physiol. 484, 791–802. https://doi.org/10.1113/jphysiol.1995.sp020704.

Peri, E., Ambrosini, E., Colombo, V.M., van de Ruit, M., Grey, M.J., Monticone, M., Ferriero, G., Pedrocchi, A., Ferrigno, G., Ferrante, S., 2017. Intra and inter-session reliability of rapid transcranial magnetic stimulation stimulus-response curves of tibialis anterior muscle in healthy older adults. PloS One 12, e0184828. https://doi.org/10.1371/journal.pone.0184828.

Pridmore, S., Filho, J.A.F., Nahas, Z., Liberatos, C., George, M.S., 1998. Motor threshold in transcranial magnetic stimulation: a comparison of a neurophysiological method and a visualization of movement method. J. ECT 14, 25–27. https://doi.org/10.1097/00124509-199803000-00004.

Rossi, S., Hallett, M., Rossini, P.M., Pascual-Leone, A., 2009. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin. Neurophysiol. 120, 2008–2039. https://doi.org/10.1016/j.clinph.2009.08.016.

Schmidt, R.A., Lee, T.D., 1999. Motor control and learning: A behavioral emphasis, 3rd ed, Motor control and learning: A behavioral emphasis, 3rd ed. Human Kinetics, Champaign, IL, US.

Šoda, J., Rogić Vidaković, M., Lorincz, J., Jerković, A., Vujović, I., 2020. A novel latency estimation algorithm of motor evoked potential signals. IEEE Access 8, 1–19. https://doi.org/10.1109/ACCESS.2020.3033075.

Stefan, K., Cohen, L.G., Duque, J., Mazzocchio, R., Celnik, P., Sawaki, L., Classen, J., 2005. Formation of a motor memory by action observation. J. Neurosci. Res. 25 (41), 9339–9346.

Tataroglu, C., Genc, A., Idiman, E., Cakmur, R., Idiman, F., 2004. Cortical relay time for long latency reflexes in patients with definite multiple sclerosis. Can. J. Neurol. Sci. 31, 229–234. https://doi.org/10.1017/S0317167100120578.

Wassermann, E.M., McShane, L.M., Hallett, M., Cohen, L.G., 1992. Noninvasive mapping of muscle representations in human motor cortex. Electroencephalogr. Clin. Neurophysiol. 85, 1–8. https://doi.org/10.1016/0168-5597(92)90094-r.