


Test-Retest Reliability and Agreement of Single Pulse Transcranial Magnetic Stimulation (TMS) for Measuring Activity in Motor Cortex in Patients With Acute Ischemic Stroke

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Busk Henriette^{1,2} , Nilsen Marianne¹, Pedersen Julie Rønne³, Kristensen Malene Glavin², Kjær Troels Wesenberg², Skou Søren Thorgaard^{1,3} and Wienecke Troels^{2,4}

¹The Research Unit PROgrez, Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Region Zealand, Slagelse, Denmark. ²Department of Neurology, Zealand University Hospital, Roskilde, Sjælland, Denmark. ³Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Syddanmark, Denmark. ⁴Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.

ABSTRACT

BACKGROUND: Transcranial magnetic stimulation (TMS) is often used to examine neurophysiology. We aimed to investigate the inter-rater reliability and agreement of single pulse TMS in hospitalised acute ischemic stroke patients.

METHODS: Thirty-one patients with first-time acute ischemic stroke (median age 72 (IQR 64-75), 35% females) underwent TMS motor threshold (MT) assessment in 4 muscles bilaterally, conducted by 1 of 2 physiotherapists. Test-retest reliability was evaluated using a two-way random effects model (2,1) absolute agreement-type Interclass Correlation Coefficient (ICC). Standard Error of Measurement (SEM) and Smallest Detectable Change (SDC) were used to evaluate agreement.

RESULTS: Reliability, SEM, and SDC of TMS was found to be moderate in right opponens pollicis (0.78 [CI 95% 0.55-0.89], SEM: 4.51, SDC: 12.51), good in right vastus medialis and tibial anterior (0.88 [CI 95% 0.72-0.96], SEM: 2.89, SDC: 8.01 and 0.88 [CI 95% 0.76-0.94], SEM: 2.88, SDC: 7.98 respectively), and excellent in right and left biceps brachii (0.98 [CI 95% 0.96-0.99], SEM: 1.79 SDC: 4.96, and 0.94 [CI 95% 0.89-0.97], SEM: 2.17 SDC: 6.01), opponens pollicis (0.92 [CI 95% 0.83-0.96], SEM: 2.68 SDC: 8.26, vastus medialis (0.92 [CI 95% 0.84-0.96], SEM: 2.87 SDC: 7.95), and tibial anterior (0.93 [CI 95% 0.86-0.96], SEM: 2.51 SDC: 6.95).

CONCLUSION: The TMS demonstrated moderate to excellent inter-rater reliability confirming the ability of these measures to reliably discriminate between individuals in the current study sample. Improvements of less than 4.96 to 12.51 could be a result of measurement error and may therefore not be considered a true change.

KEYWORDS: Acute ischemic stroke, transcranial magnetic stimulation (TMS), single pulse, motor evoked potentials (MEP), motor threshold (MT), reliability, agreement

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CORRESPONDING AUTHOR: Busk Henriette, Department of Neurology, Zealand University Hospital, Sygehusvej 10, Roskilde DK 4000, Denmark.
Email: habusk@mail.dk

Introduction

Stroke is a cerebrovascular disorder caused by a disruption of the blood supply to the brain.¹ Survivors often experience daily life disability² and some of the most frequent impairments include hemiparesis and disabled motor function.³ To relearn these motor skills, rehabilitative efforts are essential.^{4,5}

Both the acute phase post stroke (1-7 days⁶) and sub-acute phase (1 week to 6 months⁶) is associated with enhanced neural plasticity^{7,8} and recovery of motor function and functionality.⁹⁻¹² These phases are therefore recommendable targets for recovery trials.^{6,13-15}

Transcranial Magnetic Stimulation (TMS) is a non-invasive and painless technique which, when applied over the primary motor cortex, generates a descending volley in the corticospinal pathway and elicits a motor evoked potential (MEP) in the contralateral limbs muscles.¹⁶ The excitability of the corticospinal output is activated when the motor threshold (MT) is elicited. MT corresponds to the minimal intensity at which TMS evokes a contralateral motor response.¹⁷ TMS has gained ground in clinical use in the last decade and is a useful method to examine corticospinal excitability (CSE) and thereby evaluate how locomotion is impacted in neurological



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illnesses.¹⁸ TMS is typically used as a tool to monitor neurophysiological changes over time^{19,20} or as a valuable tool in predicting recovery of motor function after stroke.^{21,22}

In relation to stroke, the clinimetric properties of TMS-measured activity of the motor cortex have been investigated in chronic ischemic stroke survivors (>6 months post stroke).²³⁻²⁵ However, the reliability and agreement of TMS in acute ischemic stroke remain unexplored. A previous study found that the measurement error of functional performance tests in the acute phase post stroke was high, likely due to the quickly changing neurological impairments,²⁶ suggesting that the reliability and agreement of TMS outcome measurements might also be affected in the acute phase.

Therefore, to optimise the use of objectively measured activity in the motoric cortex, the aim of this study was to investigate the inter-rater reliability and agreement of single pulse TMS as an instrument for measuring excitability of the motor cortex in patients with acute, first-time ischemic stroke.

Methods

The study was designed as an inter-rater, inter-day reliability study, following the Guidelines for Reporting Reliability and Agreement Studies (GRASS).²⁷ The patients were included and tested the day after onset of stroke and retested the following day.

Reproducibility

Reproducibility is a concept that encompasses both measurement error and reliability.²⁸ Reliability associates measurement error to the variability between study participants and establish the measurement's discriminative ability on a group level.^{28,29} Agreement refers to the measurement inaccuracy alone, and it defines how responsive a measurement tool is to identify change over time on a personal level.²⁸ When determining the effects of a treatment on a patient population both reliability and agreement of a result are considered critical.²⁸

Ethics

The Research Ethics Committee of Region Zealand, Denmark (SJ-665) and the Danish Data Protection Agency both authorized this study without any changes (REG-231-2018). Prior to being included in the trial, all patients supplied written informed consent in accordance with the Declaration of Helsinki. Detailed information of the TMS measurement-sessions was given to the participant prior test.

Participants

Subjects were consecutively recruited through daily review of the hospital patient records at Neurovascular Centre N80 at the Zealand University Hospital (Roskilde, Denmark) between March and November 2019. Eligibility assessment was performed by 1 of the 2 raters in accordance with pre-defined inclusion and exclusion criteria for participation in the study.

Patients were eligible for inclusion if they had suffered acute ischemic cerebral stroke verified by Computer Tomography or Magnetic Resonance Imaging (1), with debut of symptoms ≤ 2 days; pre-morbid Modified Ranking Scale ≤ 1 ³⁰; had arm or leg paresis (manual muscle testing 2-4)³¹; sufficient cognitive function to participate in the study as per the assessment of either a speech therapist, a physiotherapist, or a nurse; and lastly were consistent right-handers according to the 10-item version of the Edinburgh Handedness Inventory (mean laterality index = 100).³² Patients were excluded if they had untreated drug or alcohol abuse; untreated depression; intracranial haemorrhages; global aphasia; newly discovered cancer or cancer metastasis; intracranial metal clips; pacemaker, Implantable Cardioverter Defibrillator, Deep Brain Stimulator and Vagus Nerve Stimulator or other electronic equipment; epilepsy, pregnancy; splints of metal in the eye; unstable fractures in cervical column³³; and were under the age of 18 years or unable to understand verbal or written information in Danish.

Procedures

Single pulse TMS is one stimulus applied at a time to illicit a MEP expressing the motor threshold (MT).³³ MT is the minimum stimulation intensity that can produce a motor output of a given amplitude from a muscle at rest.³⁴ In this study focusing on MT, MEPs were recognised using surface electromyography (sEMG) where the higher MEP amplitude gives the higher sEMG responses.^{35,36} Electrodes were placed over the muscles: biceps brachii, opponens pollicis, vastus medialis, and tibialis anterior at right side (DEX) and left side (SIN).^{18,37,38} All muscles were tested while resting, and with EMG confirming no muscle activity. MEP was obtained using a Magnetic Stimulator (MagLite-r25) combined with a coil connector and recorded with Keypoint.NET 2.32 Dantec (Supplemental Appendix 2). Window size was set to 5 ms, 2 mV, 2 mV for the upper limb (UL) and 10 ms, 2 mV, 5 mV for the lower limb (LL). Patients were lying in supine position on a treatment bench, with the MagLite-r25, 10 cm in diameter circular coil and the computer monitoring EMG placed as close to the main assessor as possible in order to minimize movement of the coil during testing.

All equipment was CE-marked and approved for measuring CSE, obtained with TMS MT.

Position of Motoric Cortex (M1)

The approximate position of the motoric cortex (M1) was located by measuring 'vertex', as of the point where the line between nasion toinion crosses the line between tragus to tragus in ear, bilaterally.³⁹ With the motor cortex as a focal point a standardized map of stimulation targets were used⁴⁰ and test stimulations verified by EMG to determine exact stimulation target for the individual muscle. No individual brain imaging and navigation system to determine the exact cortical location of a TMS target was implemented.

TMS

MEP was obtained by TMS-induced biphasic pulse stimulus through the magnetic coil placed 1.5 cm anteriorly of M1.⁴¹ The test was carried out as an MT-estimate (0–100), with the lowest MT and MEP amplitude consistently determined over a series of repeated single stimulus runs in targeted muscles, as an expression of motor cortex activity. Starting at 10% of max, the stimulus intensity was increased by 5% for each single pulse until MT was discovered.^{41,42} The level of MT intensity was recorded and, without modifying the coil's positioning or angling, repeated in 10 following stimulations, each at the same intensity level, in an attempt to duplicate the lowest MT-response. Throughout the measurements of each extremity, the coil was put in the indicated vertex-area and maintained with a firm, steady hand. After each TMS measurement session, data was kept in Keypoint.

EMG

EMG was used to record resting and non-voluntary muscle activity peripherally and bilaterally on the muscles of interest.^{18,37,38} Prior EMG recording, standard skin preparation procedure for cleaning and abrading was performed at each spot of the sEMG sensor placement in reference to targeted muscles.⁴³

EMG was recorded in all 4 extremities using ALPINE bioMed Pre-Gelled Disposable Surface Electrodes in combination with Ambu Neuroline Ground Neurology Surface Electrodes, one extremity at a time and independent of affected extremities. Both the active and reference electrodes were placed above the muscle belly and the nearest projection bone, with two 2 m Hush Shielded wires connecting them (Alpine Biomed). When assessing EMG in the upper limb, the ground electrode was put above the most prominent point of acromion, and when assessing EMG in the lower limb, the ground electrode was positioned above the anterior superior iliac spine.

Raters

Two physiotherapists trained in study procedures (HB, MN) performed the assessments independently. The patient was tested and retested by the rater present at the stroke unit on the respective day; because of this, in a few cases, it was the same rater doing both test and retest. It was impossible to apply a fixed schedule of rater one performing tests and rater 2 performing re-tests since the patients were acutely hospitalised and the raters were only engaged part-time. Both raters received extensive training and performed pilot testing on 5 patients prior to the study.

Test Sessions

Patients attended one test session the day after onset of stroke and were retested the following day. Three repeated stimuli runs were performed on each test session. To eliminate diurnal variation, each individual was, if possible, tested at the same time both days.⁴¹

Time interval between each single pulse or stimuli, in literature described as inter-pulse-interval (IPI), was set to last for a minimum of 10 seconds in order to achieve larger MEP amplitude, as recommended by Vaseghi et al.⁴¹ Originally both test sessions were supposed to be done twice the first day, but pilot tests with 2 test sessions per day made it clear that participants dropped out on the second test session due to exhaustion and/or stress.

Subjects were evaluated in a separate room and to ensure the patients' privacy and relaxation, doors and windows were covered to keep out light and disturbances. During the testing, only the principal investigator and the participant were present.

Age, sex, Body Mass Index (BMI), stroke severity (Scandinavian Stroke Scale)⁴⁴ and modified Rankin Scale³⁰ were collected from patients' medical records prior to the first test session. Serious adverse events and adverse events (seizures, headaches, muscle cramps, nausea and changes in neurological signs³³) were identified according to the definition established by the US food and Drug Administration⁴⁵ either on-site or in the hospital records. The test findings were recorded on a case report form and placed in a locked box as soon as the tests were completed, keeping it inaccessible until all tests were completed. The rater performing the retest was unable to examine the results from the first test.

Sample Size

The sample size in this study was a convenience sample on the basis of the eligible patients in the 9 months recruitment period.

Statistical Analysis

Descriptive statistics and plots to visualise for normality were performed for all variables. To evaluate whether there were any significant differences between the test and retest, paired t-tests were utilized, using a significance level of $P \leq .05$.

Inter-Rater Reliability

Inter-rater reliability of TMS was assessed using a two-way random effects, single-measures model (2,1) absolute agreement type, interclass coefficient (ICC).⁴⁶ The ICCs were classified using the following categories: <0.5 = poor reliability; $0.5 - <0.75$ = Moderate reliability; $0.75 - 0.9$ = Good reliability; >0.9 = Excellent reliability.⁴⁷ The acceptable level of ICC was set at a minimal level of 0.75.⁴⁸

Agreement

Agreement was evaluated to establish the variability of repeated measurements when applied on an individual person level, using the actual units of the measurements. First, the Standard Error of Measurement (SEM) was calculated using the following equation: Standard Deviation (mean of test 1 score and test 2 score) $\times \sqrt{1 - R}$.⁴⁹ The variability between repeated measurements is represented by SEM, which covers 68% of future measurements. This means that there is a 68% probability that the true score lays within the interval of the SEM when repeating the measurement. From the SEM, the Smallest Detectable

Table 1. Patient characteristics n=31 (20 male, 11 female).

SEX (FEMALE), N (%)	11 (35)
Age, years; median (IQR)	72 (64-75)
Body Mass Index, kg/m ² ; mean (SD) ^a	25.6 (3.4)
Infarction site (right hemisphere), n (%)	17 (54)
Thrombolysis (yes), n (%) ^a	12 (41)
Diabetes Mellitus (yes), n (%)	4 (13)
*Scandinavian Stroke Scale; mean (SD)	49.4 (5.3)
**Scandinavian Stroke Scale –arm, hand, leg; mean (SD)	15.9 (1.3)

^aMissing data n=2.

*Scandinavian Stroke Score. Scale from 0 to 58 point, 58 is maximum.

**SSS-arm, hand, leg scores 0 to 18, 18 is maximum.

Change (SDC) at 95% level was calculated using the following equation: $SDC = SEM \times 1.96 \times \sqrt{2}$.²⁷ The SDC also represents the variability between repeated measures, but increases the likelihood of finding the true score within the interval by covering 95% of future measurements. In order to represent a meaningful change in test performance rather than test-retest variability alone, variations on repeated measures must surpass these predicted agreement intervals, depending on the degree of probability used SEM.⁵⁰ For the TMS-test results, Bland-Altman plots were created by graphing the difference between test and retest against the mean of test and retest scores with 95% Limits of Agreement to visualize any systematic bias between the 2 sessions.⁵¹

The statistical analysis was performed in Stata version 17 (StataCorp LLC, Texas, USA) and Bland-Altman plots were created using SPSS (IBM SPSS, New York, USA).

Results

Demographic data

During the time of recruitment, 36 patients were found eligible for participation. The first 5 included patients were used in the pilot tests to standardise procedures before this study. Thirty-one patients were included in the analysis (Table 1).

The 31 patients had a median age of 72 years and 35% were female. Patient characteristics are presented in Table 1. All the included patients responded to the stimulation and were able to evoking the MEP. For stimulation parameters evoking the MEP see Bland Altman plots. No adverse events were reported.

Inter-rater reliability analysis

The inter-rater reliability of opponens pollicis (DXT) was moderate with ICC(2,1) of 0.78 [CI 95% 0.55-0.89]. The vastus medialis (DXT) and tibialis anterior (DXT) was good with ICC(2,1) of 0.88 [CI 95% 0.72-0.96] and 0.88 [CI 95% 0.76-0.94], respectively. The 5 remaining muscles had excellent

inter-rater reliability with ICC(2,1) 0.98 [CI 95% 0.96-0.99] for the biceps brachii (DXT), 0.94 [CI 95% 0.89-0.97] for the biceps brachii (SIN), 0.92 [CI 95% 0.83-0.96] for the opponens pollicis (SIN), 0.92 [CI 95% 0.84-0.96] for the vastus medialis (SIN) and 0.93 [CI 95% 0.86-0.96] for the tibialis anterior (SIN). All ICCs were found acceptable according to the pre-specified level (see Tables 2 and 3).

Agreement

The Bland-Altman plots did not reveal any clear tendencies of heteroscedasticity since the plots were uniformly spread across different values on the x-axis. For all tests, the difference between the test and the retest was not significant. The difference between test and retest plotted against the mean of test to retest for visualisation of systematic bias is presented in Bland-Altman plots in Supplemental Appendix A.

The B-A plots revealed that opponens (DXT + SIN), vastus medialis (SIN) and one in the vastus medialis (DXT). (Figures 3-6 (Supplemental Appendix)) all contained 2 outliers in the B-A plot.

The SEM_{Agreement} was 1.79 and the SDC 4.96 for the biceps brachii (DXT), respectively. Likewise 2.17 and 6.01 for the biceps brachii (SIN), 4.51 and 12.51 for the opponens pollicis (DXT), 2.68 and 8.26 for the opponens pollicis (SIN), 2.89 and 8.01 for the vastus medialis (DXT), 2.87 and 7.95 for the vastus medialis (SIN), 2.88 and 7.98 for the tibialis anterior (DXT) and 2.51 and 6.95 tibialis anterior (SIN) (Table 3).

Discussion

We found excellent inter-rater reliability and agreement in 5 muscles (biceps brachii (DXT), biceps brachii (SIN), opponens (SIN), vastus medialis (SIN) and tibialis anterior (SIN)), good reliability and agreement in 2 muscles (vastus medialis (DXT) and tibialis anterior (DXT)) and moderate inter-rater reliability and agreement in one muscle (opponens pollicis (DXT)).

To our knowledge, this is the first study to evaluate inter-rater reliability and agreement of single pulse TMS as an instrument for measuring the excitability of the MEP when activated by the motor threshold (MT) in patients in the acute phase after stroke. Earlier work with patients in the subacute and chronic stages of stroke showed that TMS MEP measured at the tibialis anterior muscle was reliable with excellent ICC.^{19,38} Similarly, Schambra et al found reliability to be excellent in subacute stroke patients when surface EMG was obtained from bilateral first dorsal interosseous muscles (17.4 ± 9.8 days post stroke).¹⁹

Numerous studies have investigated test-retest agreement of TMS MEP in patients with stroke. In the tibialis anterior muscle, reported SEM estimates range from 2.2 to 2.07¹⁹ while SDC has been reported to be 5.75 in patients in the chronic phase after stroke. In the subacute phase (17.4 ± 9.8 days post stroke), Caccio et al reported a SEM value of 2.41 [95% CI: 0.99-3.64] and a SDC value of 6.67 [95% CI: 2.75-10.08]

Table 2. Reliability measures of the TMS test-retest, n=31.

AREA	INTRACLASS CORRELATION COEFFICIENT (95% CI)	STANDARD ERROR OF MEASUREMENT	MINIMAL DETECTABLE CHANGE
Biceps brachii (DXT)	0.98 (0.96-0.99)	1.79	4.96
Biceps brachii (SIN)	0.94 (0.89-0.97)	2.17	6.01
Opponens (DXT)	0.78 (0.55-0.89)	4.51	12.51
Opponens (SIN)	0.92 (0.83-0.96)	2.68	8.26
Vastus medialis (DXT)	0.88 (0.72-0.96)	2.89	8.01
Vastus medialis (SIN)	0.92 (0.84-0.96)	2.87	7.95
Tibialis anterior (DXT)	0.88 (0.76-0.94)	2.88	7.98
Tibialis anterior (SIN)	0.93 (0.86-0.96)	2.51	6.95

Abbreviations: DXT = right hemisphere; SIN = left hemisphere.

Table 3. Test-Retest Reliability and Agreement of single pulse Transcranial Magnetic Stimulation (TMS): ICC, SEM and SDC n=31.

AREA	MEAN DIFFERENCE	LOWER LIMIT OF AGREEMENT	UPPER LIMIT OF AGREEMENT
Biceps brachii (DXT)	-0.81	-7.55	5.93
Biceps brachii (SIN)	-0.16	-8.35	8.03
Opponens (DXT)	-3.39	-20.05	13.27
Opponens (SIN)	0.16	-10.40	10.72
Vastus medialis (DXT)	-2.58	-12.96	7.80
Vastus medialis (SIN)	0.97	-9.88	11.82
Tibialis anterior (DXT)	1.13	-9.80	12.06
Tibialis anterior (SIN)	-0.32	-10.08	9.44

Abbreviations: DXT = right hemisphere; SIN = left hemisphere.

measured in the first dorsal interosseous muscles.^{19,38} These findings indicate that TMS is a reliable and relevant measure in the acute, subacute and chronic phases after stroke. A novel TMS-EEG procedure has found success in evoking MEP in chronic stroke patients impossible to MEP-evoked, and this procedure has also been found reliable.⁵²

The relatively lower reliability in the DXT opponens pollicis, DXT vastus medialis and DXT tibialis anterior in our study might indicate that the non-dominant (right-side) were more reliable than the dominant (left-side) hemisphere. This has also been found in previous studies.^{19,53} It has been suggested that the left hemisphere is more excitable as it relates to the dominant side, and therefore might be less reliable in tests.⁵³

TMS is suggested as a reliable measure for activity in the motor cortex in the acute phase post stroke⁵⁴ where day-to-day variation in measures in functionality was found to be unrelated to physiological measures in the first 3 weeks. TMS is thus a valid internal measure in the acute phase, as opposed to physical tests in the same phase which rarely are.²⁶

Clinical Interpretation

Choosing the level of certainty

The absolute reliability measure SEM provides a 68% probability that an actual change lies within the estimated range when repeating the measurement, while the SDC provides a 95% chance of identifying a real change.⁵⁰ We present estimates of both SEM and the SDC in our study to allow clinicians to choose which level of confidence they wish to pursue, while understanding the differences in interpretation.

When using the SDC in a clinical context, observed differences below 4.96 to 8.26 in most muscles and below 12.51 in opponens pollicis (DXT) may be a result of measurement error and not true changes in the excitability of the MT. The minor degree of measurement error, except in the opponens pollicis, which is substantial compared to other findings both in this and other studies,^{19,38} indicate that TMS is useful measuring changes very early after stroke, which can be helpful in the process of clinical reasoning and rehabilitation of the stroke survivors. This internal measure is not affected by external factors

like stress, fatigue or cognitive disorders which can affect physical performance outcomes.²⁶

The acute hospitalisation makes it difficult to have a standardised test and rater setup, and in 2 cases the rater did both the test and retest which could be a bias in case the rater remembered the test results. Another challenge with the acute hospitalisation is to create a uniform test setup with the same amount of activities before the test and retest. At the same time the spontaneous neurological recovery is quite substantial especially in the first 72 hours after stroke onset,¹³ which means that patients to some extent will spontaneously recover without rehabilitation or medicine. Despite the spontaneous neurological recovery in the acute phase post stroke, the TMS measures seem reliable.

The current understanding of brain repair processes suggests that the fastest change occurs in the first weeks to months post stroke.^{6,13} The acute post-stroke time window therefore represents a clinically important phase for treatment and research in order to facilitate optimal rehabilitation.⁶ Future studies should therefore consider interventions in the acute phase after stroke to explore a possible effect on neurorehabilitation and use the 2017 consensus-based stroke recovery and rehabilitation recommendation of TMS measures in stroke trials to achieve comparable patient characteristics and outcome measures.^{6,55,56}

Limitations

The scope of this study is limited because it only looks at inter-rater reliability and agreement. Intra-rater reliability and agreement would have been crucial to assess because it enables the measurement of reliability and agreement when only one rater is evaluating the TMS. Our setup without fixed rater setup could have influenced the measurement error since we do not know the intra-rater reliability. Our test setup, however, will most likely be the real-life situation in a given clinical setting, where clinicians work set hours rather than following each patient through their entire treatment term. As a result, the current study reflects actual practice, enhancing the external validity of the findings.

The COSMIN's guideline states that reliability studies should include patients with a stable condition, which is very difficult in acute stroke patients.²⁹ So another drawback is the possibility of day-to-day variations in post-stroke symptoms, which could alter the results and, as a result, the measurement accuracy. Originally, the test and retest were supposed to be done on the same day, however based on experiences from the pilot test testing twice in 1 day was not feasible.

We found 2 outliers in the B-A plot for the opponens (DXT + SIN), vastus medialis (SIN) and one in the vastus medialis (DXT). (Figures 3-6 (Supplemental Appendix)) A difference of 25 in MT from test to retest is substantial, and affects the SEM and SDC in especially the opponens pollicis (DXT) muscle. This could be an expression of muscle representation in the motor cortex, which is considered highly sensitive, or a result of just a minor movement of the TMS recoil,

which has major consequences for how and where MT is registered. MT and MEP were assessed subjectively and visually, which likely influenced our results. The MEP outcome could also be evaluated as MEP amplitude and latency. Future studies could consider involving MEP amplitude when measuring MT to obtain an objective score of the MTs,²¹ which would have raised the validation of our results, however was not possible in this setup. Finally, it is worth mentioning that the fact that MEPs reflect the excitability of the entire corticospinal tract and cannot be considered a pure estimate of cortical excitability is another source of bias. This is a potential source of confusion as well as an inherent limitation of MEPs.⁵⁷

Conclusion

The TMS demonstrated moderate to excellent inter-rater reliability in hospitalised patients with first-time acute ischemic stroke with ICCs_(2,1) of 0.78 (CI 95% 0.55-0.89) to 0.98 (CI 95% 0.96-0.99). Based on the current results, the threshold to detect a real change for a group and individual patients with acute stroke may be as high as 12.51 and as low as 4.96 depending on which muscle that is measured, indicating the TMS for measuring excitability of the motor cortex in patients with acute, first-time ischemic stroke having measurement error to some extent.

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Author Contributions

Conceptualization: HB, MGHK, TK, TW. Data curation: HB, JRP. Formal analysis: JRP. Funding acquisition: HB, STS, TW. Investigation: MN, HB. Methodology: HB, STS, TW. Project administration: HB. Validation: HB, MN, MGHK. Visualisation: HB. Writing – original draft: HB. Writing review and editing: HB, MN, MGHK, JRP, STS, TK and TW.

ORCID iD

Busk Henriette  <https://orcid.org/0000-0002-0376-2962>

Supplemental Material

Supplemental material for this article is available online.

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