NÖRO PSİKİYATRİ ARŞİVİ
ARCHIVES OF NEUROPSYCHIATRY

RESEARCH ARTICLE

Article No: 82

Arch Neuropsychiatry 2026;63:526–532
https://doi.org/10.29399/npa.29412

Corticospinal Excitability After Continuous and Intermittent Theta Burst Stimulation Applied on the Lateral Cerebellum: A Study on Healthy Individuals

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ABSTRACT

Introduction: To investigate the effects of continuous (cTBS) and intermittent (iTBS) theta burst stimulation applied over the lateral cerebellum on corticospinal excitability in healthy individuals.

Methods: Twenty right-handed healthy male participants underwent three TBS sessions (cTBS, iTBS, sham) in a randomized crossover design. Motor evoked potentials (MEPs), resting and active motor threshold (RMT and AMT, respectively), and cortical silent period (CSP) were assessed before and after each session using single-pulse transcranial magnetic stimulation over the left primary motor cortex. Transcranial magnetic stimulation was delivered to the right cerebellar hemisphere at 80% of active motor threshold.

Results: A significant reduction in MEP amplitude was observed following iTBS (p=0.028), while no significant changes occurred after cTBS or sham stimulation. No significant effects were found in RMT or CSP across any of the protocols. All sessions were well tolerated and considered safe. Mild and transient side effects, such as neck discomfort or headache, were reported in five participants.

Conclusion: Intermittent cerebellar TBS was associated with reduced MEP amplitude, suggesting decreased corticospinal excitability, whereas cTBS and sham stimulation did not produce significant effects. Cerebellar TBS was safe and well tolerated in all participants. These findings suggest that cerebellar iTBS may exert modulatory effects on motor cortical excitability and may contribute to a better understanding of cerebellar stimulation effects in healthy individuals.

Keywords: cerebellar TMS, cerebellum, corticospinal excitability, theta burst stimulation, transcranial magnetic stimulation

Cite this article as: Azman İste F, Yayla V, Bajrami A, Sözer N, Demirtaş Tatlıdede A, Öge AE. Corticospinal Excitability After Continuous and Intermittent Theta Burst Stimulation Applied on the Lateral Cerebellum: A Study on Healthy Individuals. Arch Neuropsychiatry 2026;63:526–532. doi: 10.29399/npa.29412

INTRODUCTION

Cerebellum plays an important role in the modification of voluntary motor movements via its outputs to motor cortex (M1). The main cerebellar efferent motor pathway is the dentatothalamocortical (DTC) tract that has facilitatory effects on the contralateral motor cortex (M1) (1). However, activation of the Purkinje cells of the cerebellar cortex inhibits the dentate nucleus, thus it results in disfacilitation of the M1.

Transcranial magnetic stimulation (TMS) is a non-invasive tool and has widely been used for the past four decades that has enabled the investigation and modulation of neural networks. It is known that repetitive TMS (rTMS) can modulate cortical excitability by causing facilitation or inhibition (or disfacilitation) depending on the applied protocol beyond the stimulation period, producing both local and distant effects in motor and non-motor brain regions. In healthy individuals, low-frequency rTMS (≤1 Hz) has inhibitory effects via adjustment of synaptic plasticity towards long term depression (LTD), while high-frequency rTMS (≥5 Hz) causes increased excitability via long term potentiation (LTP)-like mechanisms when applied over M1, based on MEP amplitude changes in most studies (2–4). It has been suggested that the increase in MEPs after high-frequency rTMS might not reflect direct excitation of the cortex, but rather a reduction in GABA-mediated intracortical inhibition (5–7). Conversely, low-frequency rTMS may enhance inhibitory effects through GABA-B–related mechanisms, which is often seen as a longer cortical silent period (8–11).

Highlights

- **Cerebellar TBS was safe and well tolerated in all participants.**
- **Cerebellar iTBS reduced MEP amplitude in healthy subjects.**
- **cTBS showed no significant effect on MEP amplitude.**

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Received Date: 30.03.2026, **Accepted Date:** 12.05.2026, **Publication Date:** 17.07.2026

Approximately two decades after the introduction of TMS, Huang et al. proposed theta burst stimulation (TBS) that is a specific, efficient and fairly consistent rTMS protocol that can induce long-lasting physiological changes. It has some advantages such as shorter stimulation durations with lower intensity compared to conventional rTMS protocols. Transcranial magnetic stimulation consists of bursts of three pulses delivered at 50 Hz, repeated every 200 ms (5 Hz) (12). Intermittent TBS typically involves a total of 600 pulses applied over approximately three minutes in an intermittent pattern (2 seconds on, 8 seconds off). When delivered over the motor cortex, iTBS has been shown to increase cortical excitability for at least 20 minutes, producing effects that resemble long-term potentiation and are comparable to those observed after high-frequency rTMS. In contrast, cTBS delivers the same number of pulses continuously over a much shorter duration (approximately 40 seconds) and is generally associated with a reduction in cortical excitability lasting up to 60 minutes. These effects are considered analogous to long-term depression and are similar to those induced by low-frequency rTMS (12). Importantly, some studies suggest that TBS protocols may produce more robust and longer-lasting neurophysiological effects than conventional rTMS paradigms (13,14).

However, the effects of these different TBS protocols applied on the cerebellum are not yet clearly understood. Although cerebellar TMS has been reported as an effective and promising method to evaluate and modulate cerebello-cortical networks**,** the current literature includes heterogenous results regarding the effects of rTMS or TBS protocols applied on cerebellum in healthy individuals. The aim of this study is to investigate cerebellar intermittent and continuous TBS effects in terms of excitability changes on contralateral M1 in healthy individuals.

METHODS

Subjects

The subjects were selected and included into the study according to safety of the TMS group guideline's criteria (15). Twenty right-handed male healthy volunteers, aged between 23 and 44, who had no history of any neurologic, psychiatric, and cardiologic disease, head trauma, no family history of epilepsy and who were not taking any drugs that may affect central nervous system (CNS) excitability were enrolled in the study. During the two days before each TBS session, subjects required sleep well and during the twelve hours of each TBS session, subjects required not to drink coffee, excessive tea, alcohol, or any drugs that may affect CNS excitability (15). All participants were chosen as male subjects because we aimed to exclude women's menstrual cycle's possible effects on cortical excitability (16). Written informed consent was obtained from all volunteers before testing. This study was approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee with file number 2014/254 on 15 December 2014.

Study Design

All subjects underwent cTBS, iTBS and sham TBS sessions and each session was performed on a separate day, at least 1 week apart. The order of the TBS protocol was determined randomly for each subject. All sessions were performed at the same time of the day (between 12:00 and 14:00). Resting motor threshold (RMT) and active motor threshold (AMT) were determined as well as motor evoked potentials (MEP) and cortical silent periods (CSP) were recorded before and immediately after each TBS session. After each procedure, all subjects were questioned regarding the tolerability and side effects of the cerebellar TBS and whether they experienced any unpleasant sensations or discomfort related to cerebellar TBS.

Electromyography (EMG) recordings

Surface EMG was recorded from the right first dorsal interosseous (FDI) muscle using 1 cm diameter surface Ag/AgCl electrodes placed according to muscle belly tendon montage technique. A circular ground electrode was placed on the dorsal surface of right wrist. The electrodes were connected to a Synergy electromyography system (Medelec, Oxford Instruments, UK). Electromyography activity was continuously monitored with auditory and visual feedback during the process. The MEPs were recorded with 2 Hz-10 kHz filter settings, and sensitivities of 50 μV-1 mV per division.

Transcranial magnetic stimulation (TMS) studies

Transcranial magnetic stimulation studies were performed with MagStim 200 (Magstim Co., Whitland, Dyfed, UK) stimulator connected to a standard figure-of-eight flat coil (70 mm diameter) placed over primary motor cortex. The figure-of-eight coil was preferred over the double-cone coil due to its better spatial selectivity, which was considered appropriate for targeting the lateral cerebellar cortex, where the distance from the scalp is relatively short. This coil configuration has been shown to be effective, easy to apply, and comfortable, and has been widely used in cerebellar TMS studies conducted in both healthy individuals and patient populations (17–21). For single-pulse TMS, the coil was placed tangentially over the left motor cortex with the handle pointing posterolaterally. To locate the motor hotspot, slightly suprathreshold stimuli were applied over the left M1, and the coil was gradually moved in ~5 mm steps until the site producing the largest and most consistent MEPs from the FDI muscle was identified. The optimum scalp position to elicit MEPs in the contralateral FDI was marked on the tight-fitting cap placed on the participant's head to assure stable coil placement throughout the session.

The RMT was defined, at the same coil position, as the lowest stimulation intensity that elicited MEPs greater than 20 μV in at least 5 out of 10 trials at rest. The AMT was the lowest stimulation intensity that evoked MEPs greater than 200 μV in at least 5 out of 10 trials while the participant maintained approximately 10–15 % of the maximum voluntary contraction, with audio-visual feedback (22).

Motor evoked potentials were recorded from the right FDI at rest following stimulation of the motor hotspot with single-pulse TMS at 120% of the RMT. Eight MEP traces were collected, with at least a

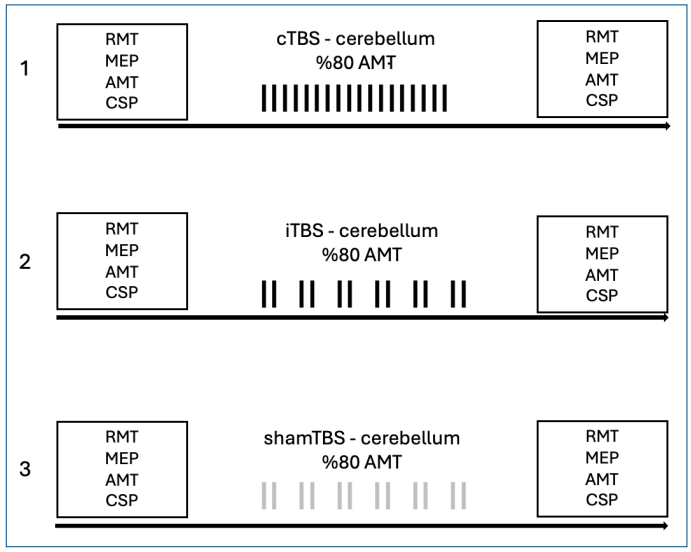

Figure 1. Schematic representation of the study design and the assessed neurophysiological parameters.

7-second interval between each stimulus to minimize residual hysteresis effects on MEP amplitude, which have been documented at inter-trial intervals as short as 5 seconds in the relaxed target muscle (3,15). Peak-to-peak amplitudes were measured, and average amplitude values were used for analysis.

The cortical silent period (CSP) was measured while participants maintained a mild to moderate voluntary contraction of the target muscle, estimated at around 20–25% of the maximal force. Transcranial magnetic stimulation pulses were applied at 140% of the AMT over the motor hotspot. Cortical silent period duration was defined as the time from the offset of the MEP to the return of voluntary EMG activity exceeding 50% of the pre-stimulus baseline following the period of EMG suppression. Twelve rectified EMG traces were recorded for each subject, and the average value was used for analysis. The sweep duration was set between 200 and 500 ms, sensitivity was adjusted to 200–500 μV/division, and a low-pass filter was 100 Hz. The order of measurements was consistent across all sessions as follows: RMT, MEP amplitude, AMT, and CSP. The whole post-TBS assessment, including RMT, MEP amplitude, AMT, and CSP, began 10 minutes after the completion of TBS and took approximately 20–25 minutes to complete, with the last measurement obtained approximately 30–35 minutes after TBS completion.

Figure 1 provides an overview of the study protocols and the neurophysiological parameters assessed.

Theta burst stimulation

Continuous and intermittent TBS were performed with a MagStim Rapid² magnetic stimulator (Magstim Co., Whitland, Dyfed, UK) connected to a standard figure-of-eight flat coil (70 mm diameter). Participants were seated in a comfortable armchair during procedure, were asked to slightly tilt their head forward for optimal coil positioning during TBS. The coil was tangentially held with the handle pointing upwards in all sessions, in a position shown as optimal for inhibition of the contralateral M1 previously (23). Theta burst stimulation was applied over the right cerebellar hemisphere, specifically by positioning the anterior intersection of two halves of the coil on a point 1 cm below and 3 cm lateral to inion as described in previous studies, which used MRI and neuronavigation, for predominantly targeting the posterior and superior lobules of cerebellum (17,24–26). The right cerebellum was selected because cerebellar output mainly influences the contralateral motor cortex. The intensity of the active repetitive stimulation was set at 80% of the AMT, consistent with previously published cerebellar TBS protocols in healthy individuals (17–19,25).

For cTBS, bursts of three pulses at 50 Hz were delivered every 200 ms for a total duration of 40 seconds, resulting in a total of 600 pulses. For iTBS, the same bursts were given in 2-second trains repeated every 10 seconds, also totaling 600 pulses (12). Sham TBS sessions were performed using a sham coil designed to mimic both the auditory and somatosensory sensations of active cTBS or iTBS, without generating effective magnetic stimulation.

Statistical Analysis

All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program version 26.0 (IBM Inc., Chicago, IL, USA). Descriptive statistics were used to summarize the pre- and post-TBS measurements.

For comparisons between pre- and post-stimulation values, the Wilcoxon signed-rank test was used, as the data did not meet the assumptions of normality. A p-value of <0.05 was considered statistically significant.

To compare the effects of the three TBS protocols, percentage changes were calculated for all parameters (MEP amplitude, CSP duration, and motor thresholds) using the formula:

((PostTBS – PreTBS) / PreTBS × 100). These changes were compared across the three conditions (iTBS, cTBS, and sham) using the Friedman test, as the data were not normally distributed**.** When the Friedman test yielded statistically significant results, pairwise comparisons were performed with the Wilcoxon signed-rank test, applying Bonferroni correction to adjust for multiple comparisons.

RESULTS

The ages of the 20 male participants ranged from 23 to 44 years, with a mean age of 31.75±5.43 years. Cerebellar TBS was well-tolerated mostly with mild side effects including neck pain and mild headache in five subjects. Severe or permanent adverse effects did not occur in any participants.

The Friedman test revealed no statistically significant difference in MEP amplitude percentage change (Post – Pre) / Pre × 100) across the three TBS protocols (p=0.705). However, within-group comparisons indicated a significant decrease in MEP amplitude following iTBS (p=0.028), whereas no significant pre-post differences were observed after either cTBS (p=0.709) or sham stimulation (p=0.681) (Figure 2A)

Analysis of RMT percentage change showed no significant differences across the stimulation protocols in the Friedman analysis (p=0.713). Similarly, Wilcoxon signed-rank tests revealed no significant within-group differences between pre- and post-stimulation values for any of the protocols (p=0.204 for cTBS, p=0.211 for iTBS, p=0.327 for sham) (Figure 2B)

A marginally significant overall difference was found for AMT (p=0.043) based on percentage changes in Friedman; however, Bonferroni-corrected pairwise comparisons did not reveal any significant differences between protocols (adjusted significance level: p <0.0167:cTBS vs. iTBS: p=0.872; cTBS vs. Sham: p=0.044; Sham vs. iTBS: p=0.048. However, Wilcoxon signed-rank analysis demonstrated a significant decrease in AMT following both cTBS (p=0.012) and iTBS (p=0.043), with no significant change after sham stimulation (p=0.471) (Figure 2C).

Cortical silent period percentage change did not differ significantly among the three TBS protocols according to the Friedman test (p=0.522). Furthermore, Wilcoxon signed-rank tests revealed no significant pre-post differences following cTBS (p=0.232), iTBS (p=0.478), or sham stimulation (p=0.799) (Figure 2D)

Table 1 summarizes the mean values, standard deviations and p-values of the measured parameters (MEP amplitude, RMT, AMT, and CSP) before and after cerebellar TBS.

DISCUSSION

In this study, we investigated the effects of cerebellar cTBS and iTBS on motor cortex excitability in healthy individuals, using single-pulse TMS measures; motor thresholds, MEPs, and CSP duration. The main findings can be summarized as follows: cerebellar iTBS led to a significant reduction in MEP amplitude, whereas cTBS did not induce a significant change in MEP amplitude. Both cTBS and iTBS protocols led to a significant reduction in AMT. However, RMT and CSP duration did not show any significant changes following either protocol. As expected, sham stimulation did not produce significant changes in any of the measured parameters implying the specificity of the observed effects and

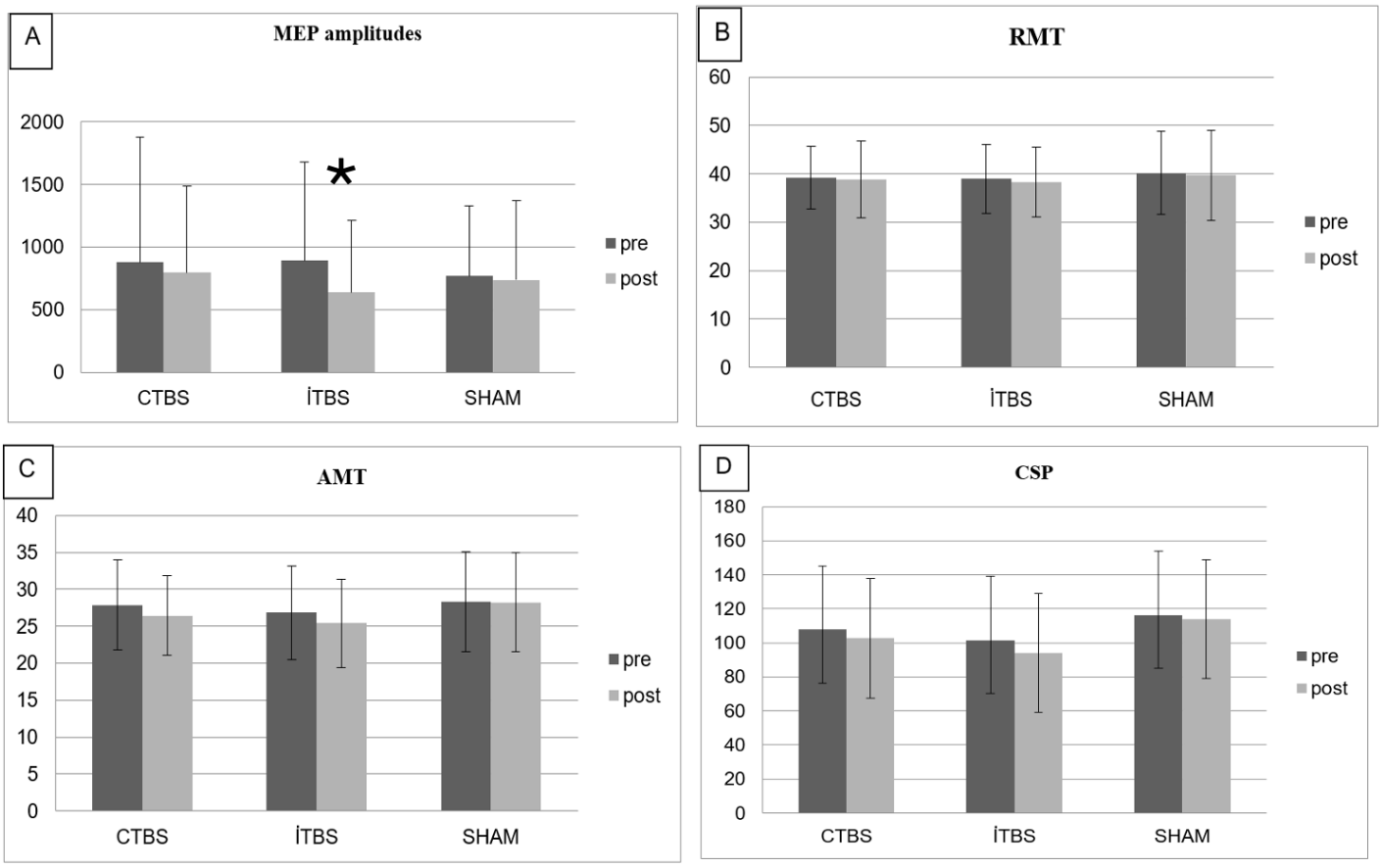

Figure 2. Pre- and post-TBS changes of measured parameters. Mean (± standard deviation) values for MEP amplitude, RMT, AMT, and CSP before and after each TBS protocol. Within-protocol comparisons were analyzed using the Wilcoxon signed-rank test. Statistically significant changes ($p < 0.05$) are indicated by an asterisk. (A) MEP amplitude: a significant reduction was observed following iTBS ($p=0.028$); no significant changes were found after cTBS or sham stimulation. (B) Resting motor threshold (RMT): no statistically significant pre-post differences were observed for any protocol ($p > 0.05$). (C) Active motor threshold (AMT): AMT significantly decreased after cTBS ($p=0.012$) and iTBS ($p=0.043$), while no change was detected following sham stimulation ($p=0.471$). (D) Cortical silent period (CSP): no significant changes were found between pre- and post-stimulation in any condition ($p > 0.05$).

Table 1. Mean values and standard deviations of measured parameters (RMT, AMT, MEPamp, CSP) of the subjects before and after cerebellar TBS

	RMT	P value	AMT	P value	MEPamp	P value	CSP	P value
cTBS								
Pre	39.3±6.5	0.204	27.9±6	0.012	879.9±999	0.709	107.6±31	0.232
Post	38.9±7.9		26.5±5.3		794.9±693		102.6±34	
iTBS								
Pre	39±7.05	0.211	26.9±6.3	0.043	890.1±788	0.028	101.5±37	0.478
Post	38.3±7.2		25.4±5.9		638.2±577		93.9±25	
ShamTBS								
Pre	40.2±8.6	0.327	28.4±6.7	0.471	769.9±559	0.681	116.2±42	0.799
Post	39.7±9.2		28.3±6.7		736.6±631		113.9±43	

AMT: Active Motor Threshold; CSP: Cortical Silent Period; cTBS: Continuous Theta-Burst Stimulation; iTBS: Intermittent Theta-Burst Stimulation; MEPamp: Motor Evoked Potential Amplitude; RMT: Resting Motor Threshold.

minimizing the likelihood of nonspecific influences such as sensory input or time-dependent variability.

The magnitude of TBS efficacy may vary depending on several factors, including stimulation frequency and intensity, total number of pulses, and individual biological differences such as brain-derived neurotrophic factor polymorphisms (27). These factors may partly account for the heterogeneous findings reported across TBS studies. Beyond the motor cortex, rTMS and TBS have also been applied to non-motor cortical regions, including the dorsolateral prefrontal cortex, superior and middle temporal gyri, and the cerebellum, in both healthy individuals and clinical populations (28). However, responses in these regions appear to be less consistent than those observed in the motor cortex, where effects can be directly assessed using well-established measures of corticospinal excitability. Within this context, we applied TBS using stimulation parameters that have been most frequently reported in the literature, using a conventional stimulation intensity previously described for cerebellar applications (17–19,25,29–31). To further reduce variability, the same participants were included across all three TBS protocols, thereby minimizing inter-individual differences. In addition, potential influences of cortisol levels and hormonal fluctuations related to the menstrual cycle were controlled by including only male participants

and by conducting all sessions at the same time of day (16,32). Notably, the absence of significant changes in any of the measured parameters following sham stimulation further supports that nonspecific effects were relatively limited in the present study.

Motor evoked potential amplitude reflects global corticospinal excitability. Intermittent TBS delivered to the motor cortex is generally associated with increased MEP amplitude and enhanced corticospinal excitability; however, cerebellar iTBS in our study resulted in a significant reduction in MEP amplitude, indicating an inhibitory or disfacilitatory effect. This finding may indirectly suggest an enhancement of cerebellar inhibitory influence on the motor cortex via the DTC pathway. Studies investigating cerebellar iTBS in healthy individuals remain limited and report heterogeneous results in the current literature (31). Both Harrington et al. and Popa et al. reported no significant modulation of MEP amplitude following cerebellar iTBS, despite differences in stimulation intensity (90% AMT and 80% AMT, respectively) (18,19). However, Koch et al. reported an increase in MEP amplitude lasting up to 15 minutes after right cerebellar iTBS, which disappeared by 30 minutes (17). Together, these findings highlight the considerable variability in MEP responses following cerebellar iTBS.

Although cerebellar cTBS has been examined more extensively than cerebellar iTBS, reported effects on MEP amplitude remain heterogeneous. In this study, cerebellar cTBS did not induce significant changes in MEP amplitude. Consistent with our findings, Popa et al. did not observe significant changes in MEP amplitude following cerebellar cTBS, despite a trend toward reduction at 10 minutes post-stimulation (18). However, several studies have reported reductions in MEP amplitude following cerebellar cTBS delivered at both 80% AMT and 90% RMT (17,19,25,30,31). In addition, MEP suppression was reported to be most prominent at 5 minutes post-stimulation and no longer significant after 45 minutes (30).

Resting motor threshold mainly reflects excitability of axons in M1 activated by TMS and no significant change in RMT was observed following either cTBS or iTBS in our study. This finding is consistent with a limited number of studies reporting similarly nonsignificant effects of these protocols on RMT (17,19,20,31,33).

The cortical silent period is defined as the temporary suppression of voluntary electromyographic activity following a TMS-induced MEP. It reflects complex inhibitory processes involving both cortical and spinal mechanisms, with possible modulation by basal ganglia circuits and various contextual or pathological factors, particularly those mediated by GABAergic neurotransmission (34). Only a limited number of studies have investigated CSP following cerebellar TMS, and consistent with our findings, no significant changes have been reported after 1 Hz rTMS, cTBS, or iTBS (19,31,35).

Overall, while cTBS is generally considered to produce effects resembling low-frequency rTMS and iTBS effects are more comparable to high-frequency rTMS, particularly in motor cortex studies, responses following cerebellar stimulation remain less consistent. Notably, some studies have suggested that iTBS responses may be relatively more consistent than those observed with cTBS (36,37). Our findings may provide additional support for previous reports suggesting that iTBS elicits more consistent physiological effects. Specifically, we observed significant changes in MEP amplitudes following iTBS, whereas cTBS did not induce considerable effects.

Although AMT is widely used as a reference parameter for determining stimulation intensity in TMS paradigms, it has not commonly been preferred as a direct outcome measure for assessing cortical excitability changes. As highlighted in a recent systematic review (38) , the majority of rTMS studies use the AMT primarily in deciding stimulation intensity, particularly in TBS protocols where 80% of AMT is conventionally applied, but do not report pre- and post-intervention AMT values (38). In our study, we observed a post-interventional decrease in AMT following both cTBS and iTBS. While this reduction might be indicative of increased excitability, its interpretation is limited by the known variability and susceptibility of AMT to non-cortical influence. Because AMT assessment is highly sensitive to multiple confounding factors including background muscle contraction, coil positioning variability, and inter-individual physiological states. Furthermore, compared to RMT, AMT exhibits greater intra-individual variability due to its dependence on sustained voluntary activation. These methodological limitations complicate its use as a reliable biomarker for neuroplastic changes. Therefore, the observed decrease in AMT may not directly indicate a true change in excitability but could instead result from methodological factors (38).

In a recent review, Hurtado-Puerto et al. evaluated the safety profile of cerebellar TMS and concluded that both cTBS and iTBS are generally safe and well tolerated (39). Across the studies, no serious adverse events were reported. However, mild and transient side effects such as neck pain, local discomfort, lightheadedness, dizziness, mild headache, tinnitus were noted in a few cases involving both healthy controls and patient populations including individuals with schizophrenia, Parkinson disease, stroke and drug-resistant epilepsy (19,40–47). Consistent with this evidence, no major adverse effects were observed in the present study. Only a few participants reported transient neck discomfort following cTBS, which did not interfere with the completion of the protocol. These findings, consistent with the existing literature, further support the favorable tolerability of cerebellar TBS when applied within recommended safety parameters.

Cerebellar rTMS has been investigated as a therapeutic tool in various neurological conditions. Improvement in motor function has been reported following cerebellar rTMS in patients with ataxia after posterior circulation stroke, as well as in spinocerebellar degeneration (48–50). In multiple system atrophy cerebellar subtype, cerebellar rTMS was shown to modulate cortical excitability and improve short-latency afferent inhibition (21). Cerebellar TBS has also been studied in Parkinson's disease, focal dystonia, schizophrenia, Alzheimer's disease, and drug-resistant epilepsy (30,33,40,43,47). These findings suggest that the cerebellum may be a valuable stimulation target beyond healthy populations, and understanding its effects in healthy individuals provides an important baseline for interpreting findings in clinical conditions.

This study has several limitations. First, a neuronavigational system was not used during stimulation. Although coil positioning followed established anatomical landmarks, the exact cerebellar regions targeted, and the specific neural populations affected remain unclear. This is a common limitation in cerebellar TBS research, where stimulation effects are often less consistent compared to motor cortex applications, likely due to anatomical and functional variability. Moreover, all outcome measures were obtained at a single post-stimulation time point, preventing the evaluation of the duration and temporal dynamics of TBS-induced effects. Additionally, the stimulation intensity for cerebellar TBS was set at 80% of the AMT of the motor cortex rather than the active brainstem threshold, which has been recommended to minimize direct corticospinal tract activation during cerebellar stimulation. However, the coil was positioned 3 cm lateral to the inion targeting the lateral cerebellar hemisphere, which reduces the likelihood of direct corticospinal tract activation, and this intensity has been widely used in previous cerebellar TBS studies in healthy individuals (17–19,25). Further, the study included only male participants, which may be seen as a limitation in terms of the generalizability of the findings to broader populations. However, this approach was intentionally adopted to minimize the potential

confounding effects of menstrual cycle-related excitability fluctuations and therefore may be considered a methodological strength in enhancing internal validity. Including paired-pulse TMS protocols such as short-interval intracortical inhibition (SICI), intracortical facilitation (ICF), and cerebellar brain inhibition (CBI) in the methodology could have provided important additional information and would enable exploration of specific intracortical and cerebellar inhibitory or facilitatory mechanisms in more detail. Furthermore, only unilateral motor cortex recordings were obtained, and potential ipsilateral or bilateral effects of cerebellar stimulation were not assessed. Lastly, a relatively small number of MEPs was recorded per condition, which may limit the reliability of the measurements given the inherent variability of MEP amplitudes. Therefore, the results should be interpreted with caution and considered exploratory. Despite these limitations, we believe that certain aspects of the study may offer useful contributions to the relevant literature. The inclusion of a sham TBS condition, which showed no measurable effects, supports the specificity of the results and strengthens internal validity. All sessions were conducted at the same time of the day to minimize circadian variability, and including a relatively larger sample compared to similar studies adds to the reliability of the findings. Most importantly, both cTBS and iTBS on cerebellum were well tolerated, with no serious adverse effects observed, confirming that cerebellar TBS can be safely applied in healthy individuals under controlled conditions.

As a result, this study supports that cerebellar TBS is safe and well tolerated in healthy individuals. The observed decrease in MEP amplitudes after cerebellar iTBS, whereas no significant changes were observed following cTBS and sham stimulation, suggests that different TBS protocols may have distinct effects on corticospinal excitability. However, these findings should be interpreted with caution due to the variability of the measures used and the limited understanding of the underlying mechanisms. As cerebellar repetitive TBS protocols are increasingly being explored for therapeutic use, the present study may contribute to future research by providing preliminary insights into their effects in healthy populations.

Acknowledgements: *The authors thank all participants for their valuable contributions and Assoc. Prof. Dr. Meyha Şahin for her assistance with statistical analyses.*

Ethics Committee Approval: This study was approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee with file number 2014/254 on 15 December 2014.

Informed Consent: Written informed consent was obtained from all volunteers before testing.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- VY, AEO; Design- FAİ, NS, VY, ADT, AEO; Supervision- NS, VY, ADT, AEO; Materials- FAİ, AB, NS, VY; Data Collection and/or Processing- FAİ, AB, NS, VY; Analysis and/or Interpretation- FAİ, VY, ADT, AEO; Literature Search- FAİ, AB, NS; Writing- FAİ, AB; Critical Reviews- VY, ADT, AEO.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: None.

REFERENCES

1. Allen GI, Tsukahara N. Cerebrocerebellar communication systems. Physiol Rev. 1974;54:957–1006. [Crossref]
2. Fitzgerald PB, Fountain S, Daskalakis ZJ. A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. Clin Neurophysiol. 2006;117:2584–2596. [Crossref]
3. Rossini PM, Burke D, Chen R, Cohen LG, 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 I. F. C. N. Committee. Clin Neurophysiol. 2015;126:1071–1107. [Crossref]
4. Siebner H, Rothwell J. Transcranial magnetic stimulation: new insights into representational cortical plasticity. Exp Brain Res. 2003;148:1–16. [Crossref]
5. Ziemann U. TMS and drugs. Clin Neurophysiol. 2004;115:1717–1729. [Crossref]
6. Wu T, Sommer M, Tergau F, Paulus W. Lasting influence of repetitive transcranial magnetic stimulation on intracortical excitability in human subjects. Neurosci Lett. 2000;287:37–40. [Crossref]
7. Di Lazzaro V, Oliviero A, Profice P, Saturno E, Pilato F, Insola A, et al. Comparison of descending volleys evoked by transcranial magnetic and electric stimulation in conscious humans. Electroencephalogr Clin Neurophysiol. 1998;109:397–401. [Crossref]
8. Lefaucheur JP, André-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol. 2014;125:2150–2206. [Crossref]
9. Daskalakis ZJ, Möller B, Christensen BK, Fitzgerald PB, Gunraj C, Chen R. The effects of repetitive transcranial magnetic stimulation on cortical inhibition in healthy human subjects. Exp Brain Res. 2006;174:403–412. [Crossref]
10. Cincotta M, Borgheresi A, Gambetti C, Balestrieri F, Rossi L, Zaccara G, et al. Suprathreshold 0. 3 Hz repetitive TMS prolongs the cortical silent period: potential implications for therapeutic trials in epilepsy. Clin Neurophysiol. 2003;114:1827–1833. [Crossref]
11. Eichhammer P, Kleinjung T, Landgrebe M, Hajak G, Langguth B. TMS for treatment of chronic tinnitus: neurobiological effects. Prog Brain Res. 2007;166:369–375. [Crossref]
12. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron. 2005;45:201–206. [Crossref]
13. Iezzi E, Suppa A, Conte A, Li Voti P, Bologna M, Berardelli A. Short-term and long-term plasticity interaction in human primary motor cortex. Eur J Neurosci. 2011;33:1908–1915. [Crossref]
14. 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. J Neurophysiol. 2011;105:2150–2156. [Crossref]
15. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009;120:2008–2039. [Crossref]
16. Smith MJ, Keel JC, Greenberg BD, Adams LF, Schmidt PJ, Rubinow DA, et al. Menstrual cycle effects on cortical excitability. Neurology. 1999;53:2069–2072. [Crossref]
17. Koch G, Mori F, Marconi B, Codecà C, Pecchioli C, Salerno S, et al. Changes in intracortical circuits of the human motor cortex following theta burst stimulation of the lateral cerebellum. Clin Neurophysiol. 2008;119:2559–2569. [Crossref]
18. Popa T, Russo M, Meunier S. Long-lasting inhibition of cerebellar output. Brain Stimul. 2010;3:161–169. [Crossref]
19. Harrington A, Hammond-Tooke GD. Theta burst stimulation of the cerebellum modifies the TMS-evoked N100 potential, a marker of GABA inhibition. PLoS One. 2015;10:e0141284. [Crossref]
20. Hardwick RM, Lesage E, Miall RC. Cerebellar transcranial magnetic stimulation: the role of coil geometry and tissue depth. Brain Stimul. 2014;7:643–649. [Crossref]
21. Yildiz FG, Saka E, Elibol B, Temucin CM. Modulation of cerebellar-cortical connections in multiple system atrophy type C by cerebellar repetitive transcranial magnetic stimulation. Neuromodulation. 2018;21:402–408. [Crossref]
22. Rothwell JC. Techniques and mechanisms of action of transcranial stimulation of the human motor cortex. J Neurosci Methods. 1997;74:113–122. [Crossref]
23. Ugawa Y, Day BL, Rothwell JC, Thompson PD, Merton PA, Marsden CD. Modulation of motor cortical excitability by electrical stimulation over the cerebellum in man. J Physiol. 1991;441:57–72. [Crossref]
24. Koch G, Oliveri M, Torriero S, Salerno S, Lo Gerfo E, Caltagirone C. Repetitive TMS of cerebellum interferes with millisecond time processing. Exp Brain Res. 2007;179:291–299. [Crossref]
25. Carrillo F, Palomar FJ, Conde V, Diaz-Corrales FJ, Porcacchia P, Fernández-Del-Olmo M, et al. Study of cerebello-thalamocortical pathway by transcranial magnetic stimulation in Parkinson's disease. Brain Stimul. 2013;6:582–589. [Crossref]
26. Del Olmo MF, Cheeran B, Koch G, Rothwell JC. Role of the cerebellum in externally paced rhythmic finger movements. J Neurophysiol. 2007;98:145–152. [Crossref]

27. Chung SW, Hill AT, Rogasch NC, Hoy KE, Fitzgerald PB. Use of theta-burst stimulation in changing excitability of motor cortex: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2016;63:43–64. [Crossref]
28. Nordmann G, Azorina V, Langguth B, Schecklmann M. A systematic review of non-motor rTMS induced motor cortex plasticity. Front Hum Neurosci. 2015;9:416. [Crossref]
29. Li Voti P, Conte A, Rocchi L, Bologna M, Khan N, Leodori G, et al. Cerebellar continuous theta-burst stimulation affects motor learning of voluntary arm movements in humans. Eur J Neurosci. 2014;39:124–131. [Crossref]
30. Bologna M, Paparella G, Fabbrini A, Leodori G, Rocchi L, Hallett M, et al. Effects of cerebellar theta-burst stimulation on arm and neck movement kinematics in patients with focal dystonia. Clin Neurophysiol. 2016;127:3472–3479. [Crossref]
31. Tremblay S, Austin D, Hannah R, Rothwell JC. Non-invasive brain stimulation as a tool to study cerebellar-M1 interactions in humans. Cerebellum Ataxias. 2016;3:19. [Crossref]
32. Clow A, Law R, Evans P, Vallence A-M, Hodyl NA, Goldsworthy MR, et al. Day differences in the cortisol awakening response predict day differences in synaptic plasticity in the brain. Stress. 2014;17:219–223. [Crossref]
33. Di Lorenzo F, Martorana A, Ponzo V, Bonnì S, D'Angelo E, Caltagirone C, et al. Cerebellar theta burst stimulation modulates short latency afferent inhibition in Alzheimer's disease patients. Front Aging Neurosci. 2013;5:2. [Crossref]
34. Zeugin D, Ionta S. Anatomo-functional origins of the cortical silent period: spotlight on the basal ganglia. Brain Sci. 2021;11:705. [Crossref]
35. Oliveri M, Koch G, Torriero S, Caltagirone C. Increased facilitation of the primary motor cortex following 1 Hz repetitive transcranial magnetic stimulation of the contralateral cerebellum in normal humans. Neurosci Lett. 2005;376:188–193. [Crossref]
36. Vernet M, Bashir S, Yoo WK, Oberman L, Mizrahi I, Ifert-Miller F, et al. Reproducibility of the effects of theta burst stimulation on motor cortical plasticity in healthy participants. Clin Neurophysiol. 2014;125:320–326. [Crossref]
37. Hinder MR, Goss EL, Fujiyama H, Canty AJ, Garry MI, Rodger J, et al. Inter- and intra-individual variability following intermittent theta burst stimulation: implications for rehabilitation and recovery. Brain Stimul. 2014;7:365–371. [Crossref]
38. Turi Z, Lenz M, Paulus W, Mittner M, Vlachos A. Selecting stimulation intensity in repetitive transcranial magnetic stimulation studies: a systematic review between 1991 and 2020. Eur J Neurosci. 2021;53:3404–3415. [Crossref]
39. Hurtado-Puerto AM, Nestor K, Eldaief M, Camprodon JA. Safety considerations for cerebellar theta burst stimulation. Clin Ther. 2020;42:1169–1190, e1161. [Crossref]
40. Demirtas-Tatlidede A, Freitas C, Cromer JR, Safar L, Ongur D, Stone WS, et al. Safety and proof of principle study of cerebellar vermal theta burst stimulation in refractory schizophrenia. Schizophr Res. 2010;124:91–100. [Crossref]
41. Argyropoulos GP, Kimiskidis VK, Papagiannopoulos S. θ-burst stimulation of the right neocerebellar vermis selectively disrupts the practice-induced acceleration of lexical decisions. Behav Neurosci. 2011;125:724–734. [Crossref]
42. Argyropoulos GP. Cerebellar theta-burst stimulation selectively enhances lexical associative priming. Cerebellum. 2011;10:540–550. [Crossref]
43. Janssen AM, Munneke MAM, Nonnekes J, van der Kraan T, Nieuwboer A, Toni I, et al. Cerebellar theta burst stimulation does not improve freezing of gait in patients with Parkinson's disease. J Neurol. 2017;264:963–972. [Crossref]
44. Erkelens IM, Bobier WR, Macmillan AC, Maione NL, Martin Calderon C, Patterson H, et al. A differential role for the posterior cerebellum in the adaptive control of convergence eye movements. Brain Stimul. 2020;13:215–228. [Crossref]
45. Demirtas-Tatlidede A, Freitas C, Pascual-Leone A, Schmahmann JD. Modulatory effects of theta burst stimulation on cerebellar nonsomatic functions. Cerebellum. 2011;10:495–503. [Crossref]
46. Richard A, Van Hamme A, Drevelle X, Golmard JL, Meunier S, Welter ML. Contribution of the supplementary motor area and the cerebellum to the anticipatory postural adjustments and execution phases of human gait initiation. Neuroscience. 2017;358:181–189. [Crossref]
47. Wang YY, Ma L, Shi XJ, Liu Y, Wu DW, Hao JM, et al. Cerebellar transcranial magnetic stimulation to treat drug-resistant epilepsy: A randomized, controlled, crossover clinical trial. Epilepsia. 2025;66:240–252. [Crossref]
48. Shiga Y, Tsuda T, Itoyama Y, Shimizu H, Miyazawa KI, Jin K, et al. Transcranial magnetic stimulation alleviates truncal ataxia in spinocerebellar degeneration. J Neurol Neurosurg Psychiatry. 2002;72:124–126. [Crossref]
49. Shimizu H, Tsuda T, Shiga Y, Miyazawa K, Onodera Y, Matsuzaki M, et al. Therapeutic efficacy of transcranial magnetic stimulation for hereditary spinocerebellar degeneration. Tohoku J Exp Med. 1999;189:203–211. [Crossref]
50. Kim WS, Jung SH, Oh MK, Min YS, Lim JY, Paik NJ. Effect of repetitive transcranial magnetic stimulation over the cerebellum on patients with ataxia after posterior circulation stroke: A pilot study. J Rehabil Med. 2014;46:418–423. [Crossref]