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TRANSCRANIAL MAGNETIC STIMULATION OF THE CEREBELLUM

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Introduction. The cerebellum is a very complex structure with many motor/non-motor functions and direct and indirect connections with almost the entire central nervous system. Transcranial magnetic stimulation (TMS) is a non-invasive electrophysiological method for studying, diagnosing, and treating disorders of the nervous system. The aim of the present review is to summarise the research and potential clinical uses of cerebellar TMS.

Methods. PubMed literature search using the key words "cerebellum TMS".

Results. TMS of the cerebellum is used in two types of protocols. The first type involves the separate stimulation of the cerebellum while tracking its clinical or electrophysiological influence on motor and non-motor functions. The second involves stimulation of the cerebellum as a conditioning stimulus before stimulating the motor cortex, to monitor the electrophysiological impact of cerebellar stimulation on the motor cortex. Most studies are performed on small groups of healthy volunteers; isolated studies are performed on patients with neurological disorders (spinocerebellar ataxia, migraine, dystonia, Miller Fisher syndrome). It has been shown that cerebellar TMS is able to influence motor systems, memory, and perception of time, and there is evidence of its electrophysiological effects in the frontal cortex.

Conclusion. Published studies suggest that cerebellar TMS is currently only important in research. There is not yet any clear or reliable evidence of the therapeutic effects of cerebellar TMS. However, its use as a treatment method can be anticipated.

INTRODUCTION

The cerebellum is a multi-functional complex structure, with direct and indirect connections with almost the entire central nervous system. Anatomically, it is associated with all parts of the brainstem via the cerebral, superior, middle, and inferior peduncles. Cerebellar grey matter is found in the cortex and its nuclei (nucleus dentatus, emboliformis, globosus and fastigii). Afferent pathways (wide afferentation from the spinal cord, brain stem, and cortex) end in the Purkinje cells of the cerebellar cortex. This input stimulates the cerebellar cortex (activation). Efferent pathways of the cerebellar cortex project to cerebellar nuclei first. These are the axons of Purkinje cells and result in inhibition of cerebellar nuclei (the lateral cortex of the cerebellum projects to the nucleus dentatus). From these nuclei (excitatory projection), anatomical efferent pathways go further after crossing in the brain stem into the thalamus and numerous brainstem nuclei. From the motor nuclei of the ventral thalamus, the efferent pathways are connected with the motor cortex, and these tracks end at both excitatory and inhibitory neurons[1]. From the thalamus, some of the efferent pathways also go towards the basal ganglia which influence the extrapyramidal system. In the nuclei of the brainstem, the efferent pathways from the cerebellum are connected to the brainstem's motor functions. Thus the cerebellum is an important regulatory centre of the motor system. A lesion in these cerebellar pathways results in clinically observable cerebellar limb ataxia (impaired coordination of voluntary movement), muscular passivity (hypotonia), tremor, speech disorder (from ataxia of articulatory and respiratory muscles), extraocular disorders, and inability to perform functions such as standing and walking due to physical instability. In addition to the traditionally accepted cerebellar motor functions, recent literature has increasingly referred to the importance of the cerebellum in non-motor functions[2,3]. The anatomical basis of its importance may be its connections by afferent (tractus cortico-ponto-cerebellaris, cortico-olivo-cerebellaris, cortico-reticulo-cerebellaris) and efferent pathways (via the thalamus and by association tracks) to the frontal, parietal, temporal, and occipital cortex. The literature

ABBREVIATIONS

CBI – Cerebellar inhibition
CS – Conditioning stimulus
EEG – Electroencephalography
ICF – Intracortical facilitation
ISI – Interstimulus interval
LICI – Long interval intracortical inhibition
MEP – Motor evoked potentials
pTMS – Paired transcranial magnetic stimulation
rTMS – Repetitive transcranial magnetic stimulation
SICI – Short interval intracortical inhibition
sTMS – Single transcranial magnetic stimulation
TMS – Transcranial magnetic stimulation
TS – Test stimulus

focuses mainly on the relationship between the cerebellum and cognitive functions as attention, behaviour, memory, learning, time perception, language processing, and emotion[4,5]. Evidence of innumerable complex functional connections with the cerebellum may be found from functional magnetic resonance imaging[6], in positron emission tomography studies[7] and in electrophysiology[8]. The concept of the cerebellum participating in non-motor functions corresponds with the understanding of its effect on motor functions – altered cerebellum pathways can lead to ataxia. One example of this understanding is the hypothesis in which schizophrenia is considered to be dysmetria in thinking – a schizophrenic patient suffers from cognitive dysmetria[9].

Transcranial magnetic stimulation (TMS) is a non-invasive electrophysiological method that can be used for studying[10], diagnosing, and treating certain neurological and psychiatric disorders[11,12]. In TMS, a magnetic stimulator creates a pulsed magnetic field that induces an electric field in the targeted tissue via a stimulation coil (attached to the patient's head, with a certain range). The electric field directly interferes with the function of the central nervous system by modulating neuronal activity[10]. TMS is categorized according to the number of magnetic stimuli: stimulation with one stimulus – single transcranial magnetic stimulation (sTMS), stimulation with two stimuli – paired transcranial magnetic stimulation (pTMS), and stimulation with many pulses – repetitive transcranial magnetic stimulation (rTMS) (ref.[13]). The effect of TMS depends on a large number of factors: the type of stimulator (performance, type and construction of coil), the selected magnetic field parameters (frequency, duration of stimulus, interstimulus interval, number of pulses, field strength), the target object (target of stimulation, physiological versus pathological state of tissue, cooperation of subject), and the experience of the practitioner (navigation TMS, standard conditions). TMS modulates not only the stimulated area, but remote structures as well. The effect on distant structures is determined by anatomical connections, by hormonal connection between the stimulated area and other areas, and by hemodynamic response (at stimulation site and in remote connecting areas) (ref.[14]). For a better idea of TMS (Fig. 1 and Fig. 2).

sTMS and pTMS are used primarily for diagnostics and research[15–17]. Motor evoked potentials (MEP) are an example of sTMS – stimulation of the motor cortex evokes motor potentials in limbs. MEPs are commonly used in neurological electrophysiology laboratories to diagnose altered tracks in the first and second motoneuron. The stimulation evokes a response from the motor cortex, and the response spreads via the corticospinal tract to the target muscle. The response from the activated muscle can be read using surface electrodes. The results of these evoked potentials are used to assess whether a motor pathway is affected.

If a subthreshold conditioning stimulus (CS) of the motor cortex is followed by a suprathreshold test stimulus (TS) of the motor cortex with a 2–5 ms interstimulus interval (ISI), it is possible to observe the inhibition of the MEP that is produced by the TS. pTMS with this ISI is called SICI – short interval intracortical inhibition[19,20]. A similar suppression can be observed if a suprathreshold CS is followed by a suprathreshold TS with a 50–200 ms ISI[19,21,22] – this is called long interval intracortical inhibition (LICI). On the other hand, if CS is followed by TS with a 7–20 ms ISI[23], it is possible to observe the facilitation of MEP produced by TS – this is called intracortical facilitation (ICF). pTMS can be used in modifications other than simply stimulating the motor cortex with two pulses. For example, it is known that transcranial magnetic stimulation of the cerebellum[24,25] 5–7 ms before transcranial magnetic stimulation of the motor cortex causes

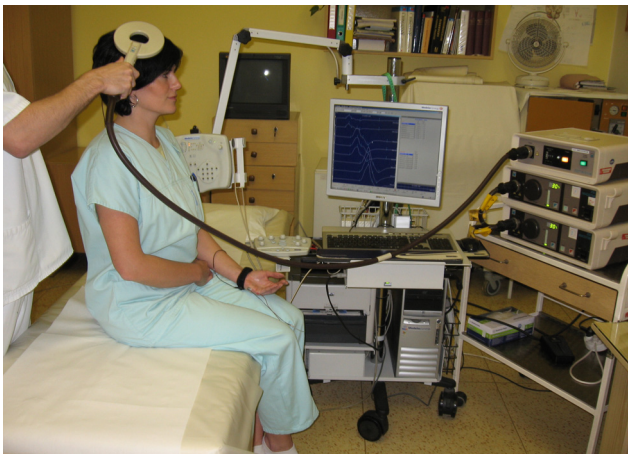

Fig. 1. Motor evoked potentials.
Using a magnetic stimulator (on the right) and a coil attached to the patient's head in the motor cortex area, we can induce evoked potentials, which can be recorded by means of surface electrodes placed over the target muscle (patient's left hand in this case).

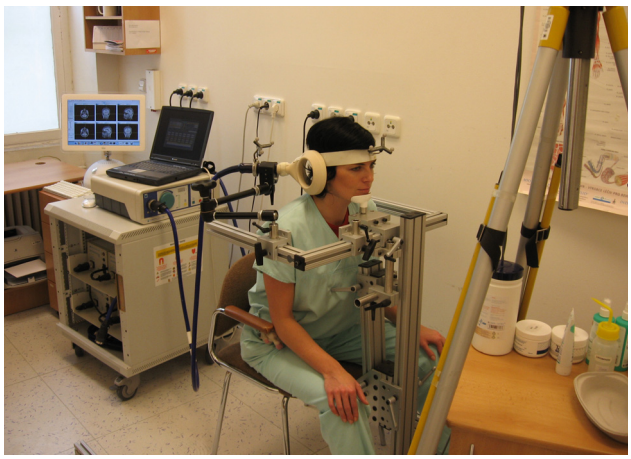

Fig. 2. Repetitive transcranial magnetic stimulation.
rTMS of the right cerebellum in a frameless navigation. Using reflective targets placed both on the coil and on the head of the patient, a camera system (not pictured) and computer software allow us to precisely focus the stimulating coil on the target structure (coil is evident from the right dorsal side of the head of the patient).

inhibition of this motor cortical stimulation. Daskalakis et al.[1] referred to this inhibition as cerebellar inhibition (CBI). rTMS of different brain areas is used in research[26] and recently as a therapeutic method (as we mentioned previously).

The aim of this review is to determine the current importance of cerebellar TMS. We were interested in how cerebellar TMS can be used for research, diagnosis, and therapeutic purposes.

METHODS

To locate information on cerebellar TMS, we used electronic information sources (publication database) PubMed at: http://www.ncbi.nlm.nih.gov/sites/entrez[27] on 22.11.2009. PubMed is a service of the United States National Library of Medicine and the National Institutes of Health. We used only the search terms "cerebellum TMS". From the 61 references found, we processed only original studies using human subjects and any type of cerebellum TMS in their protocol. We excluded one study that had only one volunteer included in its protocol.

RESULTS

We found 24 relevant publications on cerebellar TMS studies in two basic types of protocols. The first type involved separate stimulation of the cerebellum (sTMS or rTMS of cerebellum) while monitoring the clinical or electrophysiological effects of stimulation on various tasks. The second type involved the stimulation of cerebellum (sTMS or rTMS of cerebellum) as a conditioning stimulus before stimulating the motor cortex (sTMS or pTMS of motor cortex). sTMS or pTMS of the motor cortex was actually used to monitor the electrophysiological effect of this combined stimulation. The studies could also be divided according to the use of healthy subjects (most studies) or patients. A large number of published protocols monitored the effects of cerebellar TMS on motor tasks or in general on the motor system. Given the diversity of the protocols and the publication objectives, we separated this literature into five categories (A to E), and we provide basic data only: the number of subjects, whether the subjects were patients or healthy individuals, the frequency and number of stimulation pulses, the part of cerebellum stimulated, the interstimulus interval range, and the brief informative results of publications. For further details, please see the referenced literature.

A) TMS of cerebellum with healthy subjects testing motor system

A sensory-motor task after rTMS of the cerebellum was studied by Miall et al.[28] (1 Hz, 300 pulses on the right cerebellum, 28 healthy subjects). After rTMS, a test group showed significantly increased movement time of the 10-hole pegboard task. The effect lasted about 3 min and was greatest for the hand ipsilateral to the stimulation. Miall et al.[29,30] were interested in particular in movement (10 and 45 healthy subjects). The authors applied one, two, or three pulses (stimuli were separated by 50 ms) of TMS over the lateral cerebellum at the time when the subject moved his/her hand to the target. The results confirmed that all three TMS conditions used during dynamic actions resulted in a directional deviation of the reaching movement. Hashimoto et al.[31] (6 healthy subjects) and Ohtsuka et al.[32] (4 healthy subjects) investigated the effects of sTMS over the posterior cerebellum (7 mm lateral and caudal to the inion) on amplitude, velocity, and acceleration of visually guided saccadic eye movements. sTMS was able to produce hypometric saccades and abrupt deceleration if the eye movement was directed contralateral to the stimulation side of the cerebellum. On the other hand, when the eyes were moved ipsilateral to the stimulation of cerebellum, TMS produced hypermetric saccades, abrupt acceleration, and greater velocity of movement. Zangemeister et al.[33] and Nagel et al.[34] (15 healthy subjects, sTMS over the inion) studied the coordination of saccadic eye and head movements by following a visual target. With the application of sTMS under certain conditions, they found significantly shorter latencies between target presentation and commencement of saccades, increased eye movements preceding head movements, reduced or reversed delay between eye and head movements, and increased mean peak velocity of synkinetic saccades. They stated that the application of sTMS can change the central synkinesis of eye-head coordination. Sakihara et al.[35] (10 healthy subjects) used sTMS over the left lateral cerebellum side to elicit a new late electromyographic responses at the bilateral soleus muscles with a mean latency of approximately 100 ms. Lo et al.[36] (6 healthy subjects) studied the reaction time of agonists and antagonists, and the differences between their activations in a task with cancellation of motor activity of upper limb. The subjects were able to cancel activation of the biceps brachii muscle in a shorter time after sTMS over the right cerebellum. Hiraoka et al.[37] investigated the effects of cerebellar sTMS over the medial, right, and left lateral cerebellum on the triphasic electromyographic pattern. Eight healthy subjects extended the left wrist as quickly as possible in response to a start cue. sTMS was delivered over the cerebellum 50 ms after the start cue. sTMS produced a shortening of the latency in the first agonist burst, and an increase in the activity of the antagonist burst.

B) TMS of cerebellum with healthy subjects testing non-motor system

Olmo et al.[38] (1 Hz, 600 pulses; 9 healthy subjects) used rTMS over the right or left cerebellar hemisphere and studied its effect on the performance of a finger-tapping task (tapping with the right index finger for 1 min with an auditory or visual cue at 0.5–2 Hz and then tapping without a cue). rTMS of the right cerebellum ipsilateral to the movement increased the variability of the intertap interval at 2 Hz that were made while subjects were synchronizing with an auditory cue. Koch et al.[8] (17 healthy subjects) studied the perception of time with TMS in two experiments. The first experiment used 1 Hz and 600

rTMS pulses over the cerebellum, and the second used 20 Hz and 4 pulses. Immediately after rTMS, subjects reproduced the duration of visual stimulus. The authors found that 1 Hz rTMS over the left lateral cerebellum impaired time perception (overestimation) in the millisecond range. Fierro et al.[39] (10 healthy subjects) investigated the role of the cerebellum in a temporal-discrimination task without movement production. Subjects compared two paired electrical intervals, which were applied on the right forearm, and were instructed to estimate which second interval was shorter than, equal to, or longer than the first. The task was performed at baseline and after 1 Hz 900 pulses rTMS over the cerebellar hemisphere. The right cerebellar rTMS worsened temporal discrimination on the ipsilateral hand, but left rTMS did not. Desmond et al.[40] (17 healthy subjects) tested whether disruption of the right superior cerebellum impairs verbal working memory performance. sTMS was administered immediately after the presentation of a letter during the encoding phase of the trial, which was followed by a maintenance period and then by a retrieval period (second presentation of the letter). Subjects were required to press a button indicating which letter had been presented during the encoding period. Results showed no effects of sTMS on accuracy, but reaction times on correct trials were significantly increased. The authors concluded that the observed effects indicated cerebellar involvement in verbal working memory. Schutter et al.[41] (8 healthy subjects) used a lightly fluctuating frequency of about 0.2 Hz and 60 pulses over the vermis of the cerebellum. After each TMS pulse, electroencephalography (EEG) from electrodes Afz – Fp2 was recorded. There was increased theta activity in the EEG which the authors attributed to an electrophysiological link between the cerebellum and the frontal cortex.

C) TMS of cerebellum as a conditioning stimulation for TMS of motor cortex with healthy subjects

Gerschlager et al.[42] (8 healthy subjects) studied whether long-lasting effects of rTMS over the cerebellum could also be attributed to peripheral effects. They used 500 pulses with a 1 Hz frequency over the right cerebellum or over the right posterior neck. After this conditioning stimulation, the right and left motor cortex were stimulated to evoke MEP. Both of these stimulations significantly facilitated MEP in the right arm, but not in the left, for up to 30 minutes after the TMS over the cerebellum. Thus peripheral structures have a role in corticospinal excitability after rTMS. Daskalakis et al.[1] (11 healthy subjects) investigated the connection between the cerebellum and the motor cortex by examining how cerebellar TMS interacts with cortical inhibitory and excitatory circuits. CBI, SICI, LICI, and ICF were used in three experiments. The first showed that with increased TS, intensities CBI, LICI, and ICF decreased, while SICI increased. The second experiment showed that the presence of CBI reduced SICI and increased ICF. The third experiment showed that the interaction between CBI and LICI reduced CBI. The authors suggested that cerebellar stimulation results in changes to both inhibitory and excitatory neurones. Olivieri et al.[23] (10 healthy subjects) stimulated the left cerebellum with 600 pulses at 1 Hz. Before and after rTMS, they performed MEP and a paired pulse paradigm of motor cortex with ISI 1–15 ms. After rTMS, MEP from the right cortex were significantly larger, and ICF with 15 ms ISI of the right motor cortex was increased. The effect lasted for up to 30 min afterwards. Fierro et al.[43] (8 healthy subjects) explored the long-term effects of low frequency rTMS over the right cerebellum with 900 pulses at 1 Hz. Before and after cerebellar rTMS, SICI and ICF were assessed in the left motor cortex by a paired pulse paradigm (ISI 2–15 ms). The only significant modulatory effect of cerebellar stimulation was a decrease of ICF at 10 ms ISI that persisted up to 20 min after the cerebellar rTMS.

D) TMS of cerebellum with patients

Shimizu et al.[44] used rTMS with 5 seconds ISI and 10 pulses over right and left and middle of the cerebellum in 4 patients with spinocerebellar ataxia (genetically proved as SCA1,6,7) every day for 21 days. After rTMS, there were improvements in walking and balance in all 4 patients. Brighina et al.[45] (10 patients and 7 healthy subjects) applied TMS to patients with migraine. They used a CS on the right cerebellar cortex and then a TS on the contralateral motor cortex with 5–15 ms ISI. MEP were recorded from the right abductor pollicis brevis muscle. The inhibitory effects of cerebellar stimulation on the motor cortex were less in the migraine patients than healthy controls (the MEP size was higher in migraine patients). Brighina et al.[46] (8 patients and 8 healthy subjects) studied patients with focal dystonia on the upper limb and controls underwent a TMS protocol to study cerebellar brain inhibition. A cerebellar CS was followed after 5 ms by a contralateral motor cortex stimulation – TS. There were three conditions (test stimulus alone, and paired stimulation with interstimulus intervals of 2 and 10 ms). MEP were recorded from the abductor pollicis brevis muscle. Cerebellar stimulation significantly reduced MEP amplitude, increased ICF, and decreased SICI in the control subjects. In contrast, no changes in these neurophysiological measures were observed in the motor cortex of the patients. The authors suggested that there is a reduced cerebellar modulation of motor cortex excitability in patients with focal dystonia. Lo et al.[47] utilized a previously used protocol with agonist and antagonist reaction times, and the differences between their activations in a task with cancellation of motor activity of the upper limb (see above: Lo et al.[36]) with 3 patients with Miller-Fisher syndrome. The agonist (biceps) reaction time was not significantly reduced during the initial sTMS study, but significant reduction was observed during the repeat sTMS study in tandem with clinical recovery in the case of this disease (the authors previously observed this reduction in healthy subjects). In this study, there was a significant correlation between anti-GQ1b IgG titres and a change in the agonist reaction time between the initial and repeat sTMS studies. The authors suggested a role of these antibodies in attacking cerebellum fibres.

E) TMS of cerebellum and adverse events

Satow et al.[48] studied the side effects of cerebellar rTMS. They applied rTMS in 8 healthy subjects with a 0.9 Hz frequency and 900 pulses over the right cerebellum with a stimulus intensity at 90% of th e resting motor threshold (as determined by motor cortex stimulation) and with a figure-of-eight coil (stimulation with 54–76% of maximum stimulator output). There was induced nausea in two subjects, lasting 10 minutes after rTMS. This symptom was repeated on a different day in the same subjects. No other side effect was observed, including objective neurological symptoms. Brighina et al.[45] (studies listed above) reported 2 patients out of 17 subjects who had mild muscular neck stiffness. Other studies outlined above (in the categories A to D) indicates the absence of side effects or do not mention this information.

DISCUSSION

The involvement of the cerebellum in motor functional circuits is widely accepted and commonly seen in clinical practice in correlation with imaging techniques (for example, acute failure of the motor system in cerebellar stroke or chronic motor disorder in patients with spinocerebellar ataxia). Therefore it is not surprising that a large percentage of the published protocols with cerebellar TMS are directed to the motor system. From studies conducted in healthy volunteers, it is clear that cerebellar TMS can influence the motor system as accuracy of movement, coordination of muscles and pathways used for the movement, and in speed and timing of movement. Cerebellar TMS influences not only limb movement, but also extraocular movements and head movements (see results in category A). However, stimulation of peripheral structures plays a certain role in affecting the motor system alongside the stimulation of the central nervous system by cerebellar TMS[42]**.** The effect of cerebellar TMS on non-motor systems has also been repeatedly demonstrated in perception of time, the timing of motor activity, and memory (see results in category B). The protocols with clinically observable tasks (e.g. Miall et al.[28]) showed that cerebellar TMS can electrophysiologically modulate the motor cortex (see results in category C) with possible influence on both excitatory and inhibitory neurons[1]. As repeatedly demonstrated, rTMS of the cerebellum with a low frequency (1Hz) for 500–600 pulses for 30 minutes excites the contralateral motor cortex[23,42]**.**

In contrast to the large number of studies healthy volunteers, there are few studies that have used cerebellar TMS on patient populations (patients with spinocerebellar ataxia, dystonia, migraine, Miller Fisher syndrome). These focus mainly on comparing the electrophysiological impact of cerebellar TMS on the motor cortex in patients in comparison with healthy controls (see results in category D). They include studies on cortical inhibition and cortical facilitation following conditioning stimulus over the cerebellum. The impact of cerebellar TMS on motor system both in clinical and electrophysiological tests in healthy volunteers and patients, however, raises the question of the therapeutic use of this method in patients. In our review, we found only one study that tested cerebellar rTMS as a therapeutic method. For this reason we did not expect many studies on the therapeutic effect of cerebellar TMS. Shimizu et al.[44] performed cerebellar stimulation with low frequency (0.2 Hz) in 4 patients with spinocerebellar ataxia, with subsequent improvements in walking and balance. We (authors of this review) at the First Department of Neurology (St. Anne's University Hospital and Medical faculty in Brno) conducted a pilot study of rTMS over the right cerebellum (1 Hz, 600 pulses) in groups of 10 patients with early stage of Parkinson's disease[49] to influence the tone and momentum of the upper extremities (monitoring the effect by motor tests – 9 hole peg test and a Test with balls). Though there was a tendency to accelerate the movement in one of the motor tests, we found no statistically significant effects of cerebellar rTMS. Thus, the results of studies are uncertain. Either they were carried out on a very small group of patients, or they did not show any significant effects of rTMS on the motor task. In our review, we found no studies to test the therapeutic effects of cerebellar TMS on non-motor systems.

The adverse effects of cerebellar TMS as nausea were reported in a study that used a relatively high output of stimulator and 900 pulses at 0.9 Hz – Satow et al.[48]**.** The nausea was transient and not associated with neurological deficits. Adverse effects were not observed in the other studies reviewed here. Our personal experiences[49] with adverse effects are also completely negative using 600 pulses and 1 Hz. Our patients tolerated the stimulation well; no patient assessed the stimulation as painful or uncomfortable.

Overall, the protocols and objectives of current publications are very heterogeneous but not contradictory. They indicate the complexity of the influence of the cerebellum on motor and non-motor functions and increase our knowledge of this interesting structure. On the basis of the cerebellar TMS protocols, this method (including rTMS of cerebellum) can be considered as safe.

CONCLUSION

Transcranial magnetic stimulation of the cerebellum can influence the motor system, memory, and the perception of time. There is evidence of its electrophysiological effects on the frontal cortex. Based on the published studies we reviewed here, it appears that cerebellar transcranial magnetic stimulation is currently only used in research. Due to non-specific abnormal findings in different diagnostic units in studying cortical inhibition and facilitation after conditioning stimulus over the cerebellum, based on current data, we do not anticipate that cerebellar TMS will be used as a diagnostic tool in the future. The therapeutic impact of cerebellar TMS is not yet clear, but we believe that its use as a therapeutic method can be expected, rather than excluded, in the future. It is a safe method.

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REFERENCE

1. Daskalakis ZJ, Paradiso GO, Christensen BK, Fitzgerald PB, Gunraj C, Chen R. Exploring the connectivity between the cerebellum and motor cortex in humans. J Physiol 2004; 557.2: 689–700.
2. Bares M, Lungu O, Liu T, Waechter T, Gomez CM, Ashe J. Impaired predictive motor timing in patients with cerebellar disorders. Exp Brain Res 2007; 180(2):355–65.
3. Bares M, Lungu OV, Husarova I, Gescheidt T. Predictive Motor Timing Performance Dissociates Between Early Diseases of the Cerebellum and Parkinson's Disease. Cerebellum 2010; 9(1):124–135.
4. Husarova I, Bares M. Ucast cerebella na kognitivnych a nemotorickych funkciach v obraze funkcnej magnetickej rezonancie. Neurol. pro praxi 2008; 9:236–239.
5. Ohyama T, Nores WL, Murphy M, Mauk MD. What the cerebellum computes. Trends Neurosci 2003; 26(4):222–7.
6. Smith AK, Ploghaus A. Cerebellar responses during anticipation of noxious stimuli in subjects recovered from depression. Br J Psychiatr 2002; 181:411–415.
7. Speer AM, Kimbrell TA, Wassermann EM, D Repella J, Willis MW, Herscovitch P, Post RM. Opposite effects of high and low frequency rTMS on regional brain activity in depressed patients. Biol Psychiatry 2000; 48:1133–1141.
8. Koch G, Oliveri M, Torriero S, Salerno S, Gerfo EL, Caltagirone C. Repetitive TMS of cerebellum interferes with millisecond time processing. Exp Brain Res 2007; 179:291–299.
9. Andreasen NC, Nopoulos P, O'Leary DS, Miller DD, Wassink T, Flaum M. Defining the phenotype of schizophrenia: cognitive dysmetria and its neural mechanisms. Biol Psychiatry 1999; 46:908–920.
10. Bares M. Nove trendy v transkraniálni magneticke stimulaci. Neurol. pro praxi 2008; 9:79–82.
11. Lomarev MP, Kanchana S, Bara-Jimenez W, Iyer M, Wassermann EM, Hallett M. Placebo-Controlled Study of rTMS for the Treatment of Parkinson's Disease. Movement Disorders 2006; 21:325–331.
12. Kopecek M, Bares M. Repetitivní transkranialni magneticka stimulace (rTMS) v lecbe deprese. Prehled publikovanych studii. Psychiatrie 2004; 8(2):117–132.
13. Bares M, Kanovsky P, Dufek J. a kolektiv. Transkranialni magneticka stimulace. Brno: Narodni centrum osetrovatelstvi a nelekarskych zdravotnickych oboru v Brne; 2003.
14. Speer AM, Willis MW, Herscovitch P, Daube-Witherspoon M, Shelton JR, Benson BE, Post RM, Wassermann EM. Intensity-dependent regional cerebral blood flow during 1-Hz repetitive transcranial magnetic stimulation (rTMS) in healthy volunteers studied with H215O positron emission tomography: Effects of primary motor cortex rTMS. Biol Psychiatry 2003; 54:818–825.
15. Bares M, Kanovsky P, Rektor I, Hortova H. Intracortical inhibition and facilitation are impaired in early Parkinson's disease patients – a paired TMS study. Eur J Neurol 2003; 10:385–9.
16. Kanovsky P, Bares M, Streitova H, Klajblova H, Daniel P, Rektor I. Abnormalities of cortical excitability and cortical inhibition in cervical dystonia. Evidence from somatosensory evoked potentials and paired transcranial magnetic stimulation. J Neurol 2003; 250:42–50.
17. Bares M, Kanovsky P, Rektor I. Disturbed intracortical excitability in early Parkinson's disease is L-DOPA dose related: A prospective 12-month paired TMS study. Parkinsonism Relat Disord 2007; 13(8):489–94.
18. Daskalakis ZJ, Christensen BK, Fitzgerald PB, Fountain SI, Chen R. Reduced cerebellar inhibition in schizophrenia: a preliminary study. Am J Psychiatry 2005; 162(6):1203–5.
19. Nakamura H, Kitagawa H, Kawaguchi Y, Tsuji H. Intracortical facilitation and inhibition after transcranial magnetic stimulation in conscious humans. J Physiol 1997; 498:817–823.
20. Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, Wroe S, Asselman P, Marsden CD. Corticocortical inhibition in human motor cortex. J Physiol 1993; 471:501–519.
21. Valls-Sole J, Pascual-Leone A, Wassermann EM, Hallett M. Human motor evoked responses to paired transcranial magnetic stimuli. Electroencephalogr Clin Neurophysiol 1992; 85:355–364.
22. Wassermann EM, Samii A, Mercuri B, Ikoma K, Oddo D, Grill SE, et al. Responses to paired transcranial magnetic stimuli in resting, active, and recently activated muscle. Exp Brain Res 1996; 109:158–163.
23. 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(3):188–93.
24. Ugawa Y, Uesaka Y, Terao Y, Hanajima R, Kanazawa I. Magnetic stimulation over the cerebellum in humans. Ann Neurol 1995; 37(6):703–13.
25. Pinto AD, Chen R. Suppression of the motor cortex by magnetic stimulation of the cerebellum. Exp Brain Res 2001; 140(4):505–10.
26. Torriero S, Oliveri M, Koch G, Caltagirone C, Petrosini L. Interference of left and right cerebellar rTMS with procedural learning. J Cogn Neurosci 2004; 16(9):1605–11.
27. PubMed.gov U.S. National Library of Medicine National Institute of Health (2009). Available from: [http://www.ncbi.nlm.nih.gov/pubmed/]; 26.11.2009.
28. Miall RC, Christensen LO. The effect of rTMS over the cerebellum in normal human volunteers on peg-board movement performance. Neurosci Lett 2004; 371(2–3):185–9.
29. Miall RC, King D. State estimation in the cerebellum. Cerebellum 2008; 7(4):572–6.
30. Miall RC, Christensen LO, Cain O, Stanley J. Disruption of state estimation in the human lateral cerebellum. PLoS Biol 2007; 5(11):2733–44.
31. Hashimoto M, Ohtsuka K. Transcranial magnetic stimulation over the posterior cerebellum during visually guided saccades in man. Brain 1995; 118 (5):1185–93.
32. Ohtsuka K, Enoki T. Transcranial magnetic stimulation over the posterior cerebellum during smooth pursuit eye movements in man. Brain 1998; 121 (3):429–35.
33. Zangemeister WH, Nagel M.Transcranial magnetic stimulation over the cerebellum delays predictive head movements in the coordination of gaze. Acta Otolaryngol Suppl 2001; 545:140–4.
34. Nagel M, Zangemeister WH. The effect of transcranial magnetic stimulation over the cerebellum on the synkinesis of coordinated eye and head movements. J Neurol Sci 2003; 213(1–2):35–45.
35. Sakihara K, Yorifuji S, Ihara A, Izumi H, Kono K, Takahashi Y, Imaoka H, Ogino S. Transcranial magnetic stimulation over the cerebellum evokes late potential in the soleus muscle. Neurosci Res 2003; 46(2):257–62.
36. Lo YL, Fook-Chong S, Chan LL, Ong WY. Cerebellar control of motor activation and cancellation in humans: an electrophysiological study. Cerebellum 2009; 8(3):302–11.
37. Hiraoka K, Sugiyama K, Abe K.Effects of Transcranial Magnetic Stimulation Over the Cerebellum on Triphasic Electromyographic Pattern. Int J Neurosci 2009; 119(10):1523–37.
38. Del Olmo MF, Cheeran B, Koch G, Rothwell JC. Role of the cerebellum in externally paced rhythmic finger movements. J Neurophysiol 2007; 98(1):145–52.

39. Fierro B, Palermo A, Puma A, Francolini M, Panetta ML, Daniele O, Brighina F. Role of the cerebellum in time perception: a TMS study in normal subjects. J Neurol Sci 2007 263(1–2):107–12.
40. Desmond JE, Chen SH, Shieh PB. Cerebellar transcranial magnetic stimulation impairs verbal working memory. Ann Neurol 2005; 58(4):553–60.
41. Schutter DJ, van Honk J. An electrophysiological link between the cerebellum, cognition and emotion: frontal theta EEG activity to single-pulse cerebellar TMS. Neuroimage 2006; 33(4):1227–31.
42. Gerschlager W, Christensen LO, Bestmann S, Rothwell JC. rTMS over the cerebellum can increase corticospinal excitability through a spinal mechanism involving activation of peripheral nerve fibres. Clin Neurophysiol 2002; 113(9):1435–40.
43. Fierro B, Giglia G, Palermo A, Pecoraro C, Scalia S, Brighina F. Modulatory effects of 1 Hz rTMS over the cerebellum on motor cortex excitability. Exp Brain Res 2007; 176(3):440–7.
44. Shimizu H, Tsuda T, Shiga Y, Miyazawa K, Onodera Y, Matsuzaki M, Nakashima I, Furukawa K, Aoki M, Kato H, Yamazaki T, Itoyama Y. Therapeutic efficacy of transcranial magnetic stimulation for hereditary spinocerebellar degeneration. Tohoku J Exp Med 1999; 189(3):203–11.
45. Brighina F, Palermo A, Panetta ML, Daniele O, Aloisio A, Cosentino G, Fierro B. Reduced cerebellar inhibition in migraine with aura: a TMS study. Cerebellum 2009; 8(3):260–6.
46. Brighina F, Romano M, Giglia G, Saia V, Puma A, Giglia F, Fierro B. Effects of cerebellar TMS on motor cortex of patients with focal dystonia: a preliminary report. Exp Brain Res 2009; 192(4):651–6.
47. Lo YL, Fook-Chong S, Chan LL, Ong WY, Ratnagopal P. Electrophysiological evidence of cerebellar fiber system involvement in the Miller Fisher syndrome. J Neurol Sci 2010; 288(1–2):49–53.
48. Satow T, Mima T, Hara H, Oga T, Ikeda A, Hashimoto N, Shibasaki H. Nausea as a complication of low-frequency repetitive transcranial magnetic stimulation of the posterior fossa. Clin Neurophysiol 2002; 113(9):1441–3.
49. Minks E, Marecek R, Pavlik T, Choust K, Bares M. The effect of repetitive transcranial magnetic stimulation of the cerebellum on the upper limb performance in early Parkinson's disease – pilot study. Ces Slov Neurol N 2010; 73/106(1):32–36.