The Effect of Cerebellar Repetitive Transcranial Magnetic Stimulation on Electrical Brain Activity Detected by Low Resolution Electromagnetic Tomography

Efekt mozečkové repetitivní transkraniální magnetické stimulace na elektrickou aktivitu mozku detekovanou nízko-rozlišovací elektromagnetickou tomografií

MILOSLAV KOPEČEK, MARTIN BRUNOVSKÝ, TOMÁŠ NOVÁK, BARBORA TIŠLEROVÁ, JIŘÍ HORÁČEK, CYRIL HÖSCHL

Prague Psychiatric Centre
3rd Faculty of Medicine Prague, Charles University
Centre of Neuropsychiatric Studies in Prague

SUMMARY

Background: Previous studies have detected EEG, cognitive and motor cortex modulation after cerebellar repetitive Transcranial Magnetic Stimulation (rTMS). The aim of our study was to determine a) if these findings actually reflect cerebellar rTMS or rather neck muscle magnetic stimulation (MMS), and b) if cerebellar rTMS modulates frontal cortex activity. **Methods:** EEG recordings were obtained from 6 right-handed healthy volunteers before and after 1) rTMS applied over the right cerebellar hemisphere and 2) MMS applied over the right muscle trapezius. We used 20 minutes of 10 Hz rTMS and MMS with 1200 impulses. The spatial distribution of the rTMS and MMS-induced changes in the electrical brain activity were assessed using low-resolution electromagnetic tomography (LORETA). **Results:** Right cerebellar rTMS increased the power density in the delta, theta, alpha-1 and beta-2 frequency bands. Power increments in the delta, theta and beta-2 bands were found predominantly over the frontal and parietal lobes, whereas the alpha-1 power was increased bilaterally in the medial cingulate. No significant changes were detected after MMS applied over the trapezius muscle. **Conclusions:** Our results suggest the feasibility to modulate frontal cortical activity by means of cerebellar rTMS. This could support the use of the cerebellar rTMS in patients with neuropsychiatric disorders where cortico-subcortico-cerebellar abnormalities have been detected.

Key words: cerebellum, frontal cortex, parietal cortex, EEG, LORETA, rTMS

SOUHRN

Úvod: Po repetitivní transkraniální magnetické stimulaci (rTMS) mozečku byla v předchozích studiích detekována změna aktivity motorické kůry, ovlivnění kognitivních funkcí a změny na EEG. Cílem naší studie bylo ověřit: a) zda jsou tyto změny způsobené rTMS mozečku či magnetickou stimulací (MS) krčních svalů a b) zda lze po rTMS mozečku detekovat změny ve frontální kůře. **Metody:** EEG bylo provedeno u 6 zdravých dobrovolníků před a po 1) rTMS aplikované nad pravou mozečkovou hemisférou a 2) MS pravého trapézového svalu. Byla použita 20 minutová stimulace 10 Hz rTMS a MS s celkem 1200 stimuly. rTMS a MS indukovaná změna prostorové distribuce elektrické aktivity mozku byla detekována pomocí nízko-rozlišovací elektromagnetické tomografie (LORETA). **Výsledky:** Stimulace pravého mozečku zvyšovala proudovou hustotu v pásmu delta, theta, alfa-1 a beta-2. Zvýšení proudové hustoty v pásmu delta, theta a beta-2 bylo zjištěno převážně v oblasti frontální a parietální kůry. Zvýšení proudové hustoty v alfa-1 pásmu bylo detekováno bilaterálně ve středním cingulu. Po MS m. trapezius nebyly zjištěny signifikantní změny distribuce elektrické aktivity mozku. **Závěr:** Dosažené výsledky naznačují možnost modulace frontální aktivity pomocí rTMS mozečku a vytváří tak teoretický předpoklad využití rTMS mozečku u pacientů s neuropsychiatrickými poruchami, u kterých byly popsány abnormity kortiko-subkortiko-cerebelární.

Klíčová slova: mozeček, frontální kůra, parietální kůra, EEG, LORETA, rTMS

Kopeček M, Brunovský M, Novák T, Tišlerová B, Horáček J, Höschl C. The effect of cerebellar repetitive transcranial magnetic stimulation on electrical brain activity detected by low resolution electromagnetic tomography. Psychiatrie 2006; 10 (Suppl. 3): 54–58

Introduction

Recent studies showed that the cerebellum is essential not only in the coordination of movement, maintenance of balance and appropriate muscle tone but probably also in affective and cognitive processing. Schmahmann and Sherman (1998) described cerebellar cognitive affective syndrome (CCAS), named after deficits caused by cerebellar lesions. The phenomenology of patients with CCAS is similar to that of patients with frontal lesions, so functional cerebellar and frontal integration is highly probable. The functional connectivity between the cerebellum and the prefrontal cortex was suggested by neuroimaging studies during cognitive tasks which showed simultaneous activation of the cerebellum and the prefrontal cortex (Andreasen et al., 1995; Schlosser et al., 1998). The fronto-ponto-cerebellar pathways are well established, but the existence of cerebello-thalamo-prefrontal pathways were documented recently by the use of transneuronal tracer (Middleton and Strick, 2001). Using the same method Clower et al. (2001) visualised cerebello-thalamo-parietal pathway, in particular connection between the dentate nucleus and inferior parietal lobe. Neuroimaging studies have detected brain abnormalities in the cortico-subcortico-cerebellar pathway not only in neurological diseases (benign tremor, spinocerebellar ataxia) but also in primary psychiatric disorders such as depression, schizophrenia, autism, and ADHD (Rapoport, 2001).

Repetitive transcranial magnetic stimulation (rTMS) is a research tool used in neurophysiology, diagnostics and as a therapeutic method in neurology and psychiatry (Post and Keck, 2001). In rTMS, the repetitive magnetic field generated in the coil is transmitted through the scalp and scull into the brain where it induces an electrical field resulting in depolarization of neurons. Recent studies detected EEG (Schutter et al., 2003), cognitive (Desmond et al., 2005; Kopecek et al., 2004; Miall and Christensen, 2004;) and motor cortex modulation after cerebellar rTMS (Oliveri et al., 2005; Ugawa et al., 1995; Werhahn et al., 1996). However, the cerebellar rTMS also induces contraction to the neck muscles, somatosensory sensation and noise. These sensations can induce measurable changes and thus confound the results. Gerschlager et al. (2002) discussed that rTMS over the cerebellum can increase corticospinal excitability through a spinal mechanism involving activation of peripheral nerve fibres. Majority of studies use the standard sham rTMS which controls for the noise of rTMS and possibly some other nonspecific changes associated with the experiment. However, the acoustic sham does not control for muscles contraction and somatosensory sensation. The aim of our study was to evaluate the effect of cerebellar rTMS on frontal cortical activity. To control the influence of the neck muscles contraction, somatosensory sensation and the noise we used a novel active sham by repetitive magnetic stimulation (MS) applied over the right muscle trapezius.

We hypothesize that active right cerebellar 10 Hz rTMS leads to changes of neuronal electrical activity in the frontal cortex, which are detectable by EEG. EEG has a remarkably high temporal resolution (milliseconds), with spatial resolution limited to the area of the electrode sites. Pascual-Marqui et al. (1994; 1999; 2002) proposed a new approach to tackle this problem by using low resolution electromagnetic tomography (LORETA), which permits a truly three-dimensional tomography of electrical brain activity while requiring only simple constraints („smoothness of the solution“) and no predetermined knowledge about the putative number of discernible source regions.

We tested the hypothesis that rTMS over the right cerebellar hemisphere but not muscle stimulation leads to changes in the frontal activity detected by low resolution electromagnetic tomography (LORETA).

Methods

1. Subjects: We recruited 6 right handed volunteers, healthy men with a mean age 31±4.4 years. The right handedness was evaluated with the Edinburgh Handedness Inventory (Oldfield 1971). The exclusion criteria for study entry were: cardiostimulator, metal implants in the cranium, history of epilepsy, treatment for mental disorders, neurological disease, use of psychotropic drugs including amphetamines, cocaine, cannabis and/or daily intake of alcohol or similar drugs in the last month and the presence of neurological or EEG abnormalities. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The written informed consent was obtained from all subjects after the nature of the procedures had been fully explained. The local ethics committee approved the study.

2. rTMS equipment and study protocol: A high-speed Magstim Super Rapid stimulator (Magstim Company, Whitland, UK) with 70 mm eight shaped coil was used for the local rTMS administration. The coil was placed at the scalp two centimeters below and three centimeters right of the inion on the line joining the inion and the external auditory meatus with the handle of coil oriented upward vertically (Gironell et al., 2002; Daskalakis et al., 2004; Oliveri et al., 2005). A continuous air-cooling system was applied throughout the administration for optimal coil performance. Individual motor thresholds (MT) were determined using the thumb movement visualization method (Pridmore et al., 1998; Schutter et al., 2001). The MT was determined by activation of the right abductor pollicis brevis muscle. MT was determined before both active and control conditions at the same time of day. The intensity of the MT was set as the lowest strength needed to elicit 5 visual contractions within ten trials. The active stimulation condition was defined as high frequency (HF) 10 Hz rTMS over the right cerebellar hemisphere. The trains lasted for 2s with an inter-stimulus interval of 18s, with a total of 60 runs (1200 stimuli in one session). The stimulation intensity was 100% of motor threshold. These stimulation parameters were within the safety limits for rTMS (Wasserman et al., 1996). Cerebellar rTMS leads to the contraction of neck muscles, which could be uncomfortable or painful. To evaluate the influence of these adverse effects, we used the same parameters for high frequency stimulation with the coil placed over the right musculus trapezius in the middle position between the cervical spine C7 and the inner margin of the scapula as the control (sham) condition. We started with active stimulation and after more than one month we applied sham condition.

3. EEG acquisition and processing and LORETA analysis: With the use of the Brainscope amplifier system (Unimedis, Prague), nineteen-lead EEG recordings were obtained from scalp electrodes placed according to the international 10/20 system, with the reference electrode situated between electrodes Fz and Cz in the midline. The EEG signals of a 20 min. duration were recorded with the subjects in a semi recumbent position, with their eyes closed. All signals were band-pass filtered at 0.5-70 Hz and sampled with a frequency of 250 Hz. The data were stored for further off-line analysis. Before the data analysis, artifact detection was performed visually to exclude all of the EEG segments which contained obvious eye and head movements or muscle artifacts. After re-computation to an average reference, spectral analysis was performed for at least six artifact-free 5-s epochs. Since different EEG frequencies reflect different functions, data were digitally filtered into seven frequency bands according to Kubicki et al. (1979): delta (1.5-6 Hz), theta (6.5-8 Hz), alpha-1 (8.5-10 Hz), alpha-2 (10.5-12 Hz), beta-1 (12.5-18 Hz), beta-2 (18.5-21 Hz) and beta-3 (21.5-30 Hz).

Subsequently, LORETA was used to estimate the three-dimensional intracerebral current density distribution. The localization of the differences in electrical activity was assessed by voxel-by-voxel paired t-tests of the LORETA images, based on the log-transformed power of the estimated electric current density. To visualize the global, three dimensional distribution of the voxel-by-voxel t-test differences, we computed for each band the mean location center of gravity for all voxels with positive t-values and for all voxels with negative t-values. To correct it for multiple comparisons, a nonparametric single-threshold test was applied on the basis of the theory of randomization and permutation tests (Holmes et al., 1996). The omnibus null hypothesis of no activation anywhere in the brain was rejected if at least one t value (i.e. voxel, tMAX) was above the critical threshold (tCRIT) for p = 0.05 determined by 5,000 randomizations.

Results

The motor threshold before cerebellar rTMS (mean 58.8±5.9) and control muscle stimulation (mean 55.6±10.5) was not significantly different (Mann Whitney test; U=14.50, p=0.58). There were no significant differences (Mann

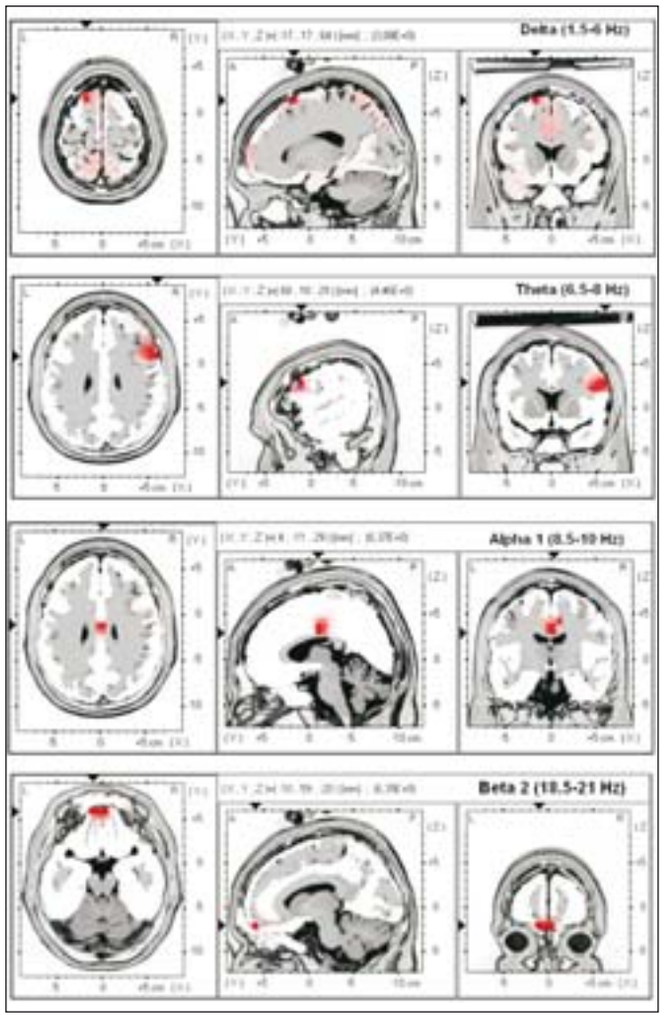

Figure 1: ***Images of voxel-by-voxel t-statistic of brain regional electrical activity using LORETA, comparing before-after cerebellar rTMS power density in 6 volunteers in delta, theta, alfa 1 and beta 2. Increased power density after cerebellar rTMS is indicated by red. The frequency band is identified in the right upper corner of each set of three orthogonal brain view in Talairach space. Structural anatomy is shown in gray scale (white-to-black). Left: axial slices, seen from above, nose up; center: sagittal slices, seen from the left; right: coronal slices, seen from the rear. The extreme t-values are given as (X,Y,Z) coordinates in Talairach space, and are graphically indicated by black triangles on the coordinate axes. Talairach coordinates: X from left (L) to right (R); Y from posterior (P) to anterior (A); Z from inferior to superior.***

Whitney test; U=10.00, p=0.24) for the intervals between the completion of the cerebellar rTMS and the start of the EEG recording (mean 887±155 s) and the intervals between the end of muscle stimulation and the start of the EEG recording (mean 1002±146 s).

After cerebellar rTMS, we detected increased power density of the delta, theta, alpha 1 and beta 2 band in many cerebral areas (Table 1). Here we describe only areas with extreme t-values for each band as well as areas expected in our hypothesis. High frequency rTMS over right cerebellum leads to increased power density of the delta band (p=0.0002) in the left superior frontal gyrus (g.), Brodmann area (BA) 6 (Figure 1), left superior, medial, middle frontal g. (BA 9, 10, 47) ($p<0.05$). The increased theta band was detected in the right inferior and middle frontal g. (BA - 9, 46) (p= 0.017) and left inferior, superior frontal g. (BA – 6, 8, 11, 46) ($p<0.05$). We detected an increased alpha1 band activity (p= 0.0002) in the medial cingulate (BA 23/24) bilaterally, and an increase of the beta 2 band (p= 0.0002) in the superior frontal g. (BA 11, 6) bilaterally (Figure 1) and in the left superior frontal g. (BA 6). After MS of the right trapezius muscle no changes in the LORETA signal were found.

Discussion

We detected marked electrophysiological cerebral changes after cerebellar rTMS, which were not observed after muscle stimulation. The effect of cerebellar rTMS lasted for up to 15 minutes. These results are in agreement with a previous study which detected changes lasting up to 30 minutes after left cerebellar rTMS and were specific for the contralateral (right) motor cortex (Oliveri et al., 2005). We proved that there are changes in the contralateral superior, middle and inferior frontal g. (BA 6, 9, 10, 47) following cerebellar rTMS. The frontal gyrus (BA 6, 9, 10) is comprised of cortical cerebellar afferents (Middleton and Strick, 2001) and activity in this area is a direct consequence of a cerebellar rTMS. Cerebellar rTMS increased power density of delta band in parietal lobe (BA 7) in agreement with recently confirmed anatomical cerebello-parietal connections (Clower et al., 2001) as well as with functional neuroimaging (Allen et al., 2005; He et al., 2004; He et al., 2006). The increased theta band was detected in similar regions as delta band, mainly in both frontal lobes and in right parietal cortex (BA 40).

Increase of the power density of the delta and theta bands, which represent inhibition processes, is in agreement with recent case reports of intermittent clinical effect of high-frequency hemispheric cerebellar rTMS for treatment drug-resistant epilepsy (Brighina et al., 2006) and reduction of seizures frequencies after high-frequency electrical stimulation of cerebellar cortex in patients with refractory epilepsy (Cooper et al., 1976; Davis 2000). Our results support the hypothesis that high frequency rTMS over cerebellum activates inhibitory influences of Purkinje cells on deep cerebellar nuclei. These, in turn, reduce their activating drive via thalamus on contralateral cerebral cortex (Ugawa et al., 1995; Brighina et al., 2006).

Some of the detected changes after cerebellar rTMS in the delta, theta, alpha-1 and beta-2 frequency bands (Table 1) must be interpreted with caution because we have no anatomical findings about cerebello-cortical projection to anterior, medial cingulate, insula, temporal or occipital lobe. It is not clear, if this changes are direct or indirect consequence of cerebellar rTMS. On the other hand, it is important to emphasize that the lack of anatomical evidence for connections between regions does not mean that the anatomical connection in question does not exist. Three recent studies using novel modality of magnetic resonance imaging (Low Frequency Fluctuation-LFF) detected functional connectivity between the cerebellum and insula (BA 13), occipital g. (BA 19), cingulate g. (BA 24), medial frontal g. (BA 8, 11, 32), hippocampus and temporal lobe (BA 21, 37, 42) (Allen et al., 2005; He et al., 2004; He et al., 2006).

The changes after rTMS were detected somewhere bilaterally, which is consistent with animal lesion, stimulation, neuroimaging and tracer studies that have shown the dentate nuclei to project bilaterally (Allen et al., 2005; Evarts and Thach, 1969; He et al., 2004; Middleton and Strick, 2001).

The excitatory activity (Beta 2 band) after high frequency cerebellar rTMS was not so large as inhibitory activity. It is not clear, if increased Beta 2 band is a direct or indirect consequence of cerebellar rTMS.

The rTMS/LORETA study present supplementary information to previously published results based on functional connectivity magnetic resonance imaging (FCMRI). FCMRI data do not directly indicate whether observed coherence signal is a reflection of afferents or efferents with respect to the brain region of interest. In our study we stimulate the cerebellum and detected changes in cortex. We suggest that observed changes present cerebellar efferents. We are not sure if the detected changes in the insula, temporal and the occipital lobe are a direct or indirect consequence of cerebellar rTMS. Because the changes are similar as those observed in the main cerebellar efferents (frontal and parietal cortex) we suggest that these changes also reflect the cerebello-cortical connections.

Our study is not the first one which used the combination of EEG and cerebellar rTMS. The only published cerebellar rTMS EEG study detected the shift in anterior asymmetry in the gamma activity from left to right dominance in the fast (30-50 Hz) EEG spectrum after high frequency (25Hz) rTMS of medial cerebellum (Schutter et al., 2003). It is difficult to compare both studies due to use of different rTMS parameters (lower frequency, higher intensity and different EEG analysis in our study).

There are several caveats to our findings. The EEG recording did not start immediately after rTMS. The volunteers had to move from rTMS lab to EEG lab and electrodes were placed exactly to the same location

Table 1: ***Brodmann areas and anatomical regions with significant increase of the power density (p<0.05, corrected) after rTMS of the right cerebellar hemisphere.***

Hemisphere/ EEG band	Lobe	Region	Brodmann area	Talairach coordinates		
				X	Y	Z
DELTA BAND						
L	Frontal	Superior Frontal g.	6	-17	17	64
L	Frontal	Medial Frontal g.	9	-10	38	22
L	Frontal	Superior Frontal g.	10	-17	66	15
L	Frontal	Medial Frontal g.	10	-3	59	8
L	Frontal	Medial Frontal g.	10	-10	59	8
R	Frontal	Superior Frontal g.	10	4	59	22
R	Frontal	Medial Frontal g.	10	4	52	8
R	Frontal	Superior Frontal g.	8	25	45	43
R	Frontal	Middle Frontal g.	8	25	31	36
R	Frontal	Middle Frontal g.	9	53	31	29
R	Frontal	Middle Frontal g.	9	39	38	36
R	Frontal	Middle Frontal g.	9	25	38	36
L	Frontal	Inferior Frontal g.	47	-52	38	-13
L	Limbic	Anterior Cingulate	24	-3	17	22
L	Limbic	Anterior Cingulate	24	-3	31	15
R	Limbic	Anterior Cingulate	24	4	31	15
L	Limbic	Anterior Cingulate	32	-3	31	22
L	Limbic	Cingulate g.	32	-10	17	29
L	Limbic	Anterior Cingulate	32	-10	31	22
L	Temporal	Superior Temporal g.	22	-59	3	-6
L	Temporal	Fusiform g.	20	-38	-25	-27
L	Temporal	Middle Temporal g.	21	-59	-53	1
L	Temporal	Middle Temporal g.	21	-66	-53	-6
L	Temporal	Sub-Gyral	21	-38	-4	-13
L	Temporal	Inferior Temporal g.	37	-59	-53	-6
L	Limbic	Parahippocampal g.	36	-24	-25	-27
L	Sub-lobar	Insula	13	-38	-4	-6
R	Limbic	Parahippocampal g.	28	18	-11	-13
L	Parietal	Superior Parietal Lobule	7	-17	-53	57
L	Parietal	Postcentral g.	7	-17	-53	71
L	Parietal	Postcentral g.	7	-10	-46	71
L	Parietal	Precuneus	7	-10	-60	36
R	Parietal	Precuneus	7	4	-60	43
L	Occipital	Cuneus	19	-10	-88	36
R	Midbrain	Mammillary Body		4	-11	-6
THETA						
R	Frontal	Inferior Frontal g.	9	60	10	29
R	Frontal	Middle Frontal g.	46	46	17	22
L	Frontal	Inferior Frontal g.	46	-52	38	8
R	Frontal	Middle Frontal g.	10	39	45	22
L	Frontal	Inferior Frontal g.	11	-24	24	-20
L	Frontal	Superior Frontal g.	6	-24	17	64
L	Frontal	Superior Frontal g.	8	-24	38	50
R	Limbic	Parahippocampal g.	36	39	-32	-27
R	Parietal	Supramarginal g.	40	60	-46	29
R	Parietal	Inferior Parietal Lobule	40	53	-46	22
ALPHA 1						
R	Frontal	Precentral g.	6	39	3	36
R	Limbic	Cingulate g.	23	4	-11	29
L	Limbic	Cingulate g.	23	-4	-11	29
R	Limbic	Cingulate g.	24	4	-11	36
L	Limbic	Cingulate g.	24	-2	-11	36
R	Parietal	Postcentral g.	3	53	-18	57
BETA 2						
L	Frontal	Superior Frontal g.	11	-3	59	-20
R	Frontal	Superior Frontal g.	11	4	59	-20
R	Frontal	Precentral g.	6	60	-4	36
R	Frontal	Superior Frontal g.	6	11	17	64
L	Frontal	Superior Frontal g.	6	-3	17	64
R	Parietal	Precuneus	7	18	-74	57
L	Parietal	Postcentral g.	7	-10	-53	71
L	Parietal	Precuneus	19	-17	-81	43
R	Parietal	Postcentral g.	3	53	-18	57
R	Parietal	Inferior Parietal Lobule	40	53	-53	43
L	Occipital	Inferior Temporal g.	37	-59	-67	1

according to the international 10/20 system. After 15 minutes interval we can loose some early changes after cerebellar rTMS. On the other hand from clinical point of view the changes lasting after 15 minutes interval could be more useful than only short intermittent changes. We navigate cerebellar rTMS using an inion as main topographic point in similar way as previous studies (Daskalakis et al., 2004; Gironell et al., 2002; Oliveri et al., 2005) and so we can conclude that we stimulate the right cerebellar hemisphere. We cannot localize the position of coil more precisely. The use of a stereotactic image guidance system could be more accurate in the future studies. Although rather small, our sample size is sufficient enough to detect EEG changes (Schutter et al., 2003; Kahkonen et al., 2005).

We did not detect any changes in the LORETA signal after MS of the right trapezius muscle. Corticospinal excitability through a spinal mechanism involving activation of peripheral nerve fibers does not induce similar effect as cerebellar rTMS. Our data provide a pilot guidance for those attempting to modulate neural activity in the cerebellum and in some of its upstream pathways using rTMS. This result suggests the possibility to use cerebellar rTMS in patients with neuropsychiatric disorders in whom cortico-subcortico-cerebellar abnormalities were detected.

Acknowledgements: *This study was supported by the project CNS: MSMT 1M0517 and MZCR VZ PCP2005 and was presented at 14th European Congress of Psychiatry of Association of European Psychiatrists in March 2006. The authors thank to Colleen Dockery Bc. and Tomas Hajek MD, PhD. for their kind help with article preparation.*

Miloslav Kopeček, MD
Prague Psychiatric Centre,
Ústavní 91, Prague 8 – Bohnice
Czech Republic
Phone: +0042 266 003 364
Fax: +0042 266 003 366
E-mail: kopecek@pcp.lf3.cuni.cz

REFERENCES

Allen, G., McColl, R., Barnard, H., Ringe, W.K., Fleckenstein, J., Cullum, C.M. Magnetic resonance imaging of cerebellar-prefrontal and cerebellar-parietal functional connectivity. Neuroimage. 2005;28, 39-48.

Andreasen, N.C., O'Leary, D.S., Cizadlo, T., Arndt S., Rezai K., Watkins G.L., Ponto L.L., Hichwa R.D. I. PET studies of memory: novel and practiced free recall of complex narratives. NeuroImage. 1995;2, 284-295.

Brighina, F., Daniele, O., Piazza, A., Giglia, G., Fierro, B. Hemispheric cerebellar rTMS to treat drug-resistant epilepsy: case reports. Neurosci Lett. 2006;397:229-33.

Cooper. I.S., Amin, I., Riklan, M., Waltz, J.M., Poon, T.P. Chronic cerebellar stimulation in epilepsy. Clinical and anatomical studies. Arch Neurol. 1976;33:559-70.

Daskalakis, Z.J., Paradiso, G.O., Christensen, B.K., Fitzgerald, P.B., Gunraj, C., Chen, R. Exploring the connectivity between the cerebellum and motor cortex in humans. J Physiology 2004;1;557(Pt 2):689-700.

Davis. R. Cerebellar stimulation for cerebral palsy spasticity, function, and seizures. Arch Med Res. 2000;31:290-9.

Desmond, J.E., Chen, S.H., Shieh, P.B. Cerebellar transcranial magnetic stimulation impairs verbal working memory. Ann. Neurol. 2005;58, 553-60.

Evarts, E.V., Thach, W.T. Motor mechanisms of the CNS: cerebrocerebellar interrelations, Annu. Rev. Physiol. 1969;31, 451–498.

Gerschlager, W., Christensen, L.O., Bestmann, S., Rothwell, J.C. rTMS over the cerebellum can increase corticospinal excitability through a spinal mechanism involving activation of peripheral nerve fibres. Clin Neurophysiol. 2002;113, 1435-40.

Gironell, A., Kulisevsky, J., Lorenzo, J., Barbanoj, M., Pascual-Sedano, B., Otermin P. Transcranial magnetic stimulation of the cerebellum in essential tremor: a controlled study. Arch Neurol. 2002;59, 413-7.

He Y., Zang Y.F., Jiang T.Z., Liang M., Gong G.L., Detecting Functional Connectivity of the Cerebellum Using Low Frequency Fluctuations (LFFs). In C. Barillot, D.R. Haynor, and P. Hellier, editors, proc. 7th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'04), part II, September 26-29, 2004, St Malo, France. Lecture Notes in Computer Science. 2004; 3217:907–915. Springer-Verlag.

He Y, Zang Y, Jiang T, Gong G, Xie S, Xiao J. Handedness-related functional connectivity using low-frequency blood oxygenation level-dependent fluctuations. Neuroreport. 2006 23; (1):5-8.

Holmes, A.P., Blair, R.C., Watson, J.D.G., Ford, I. Nonparametric analysis of statistic images from functional mapping experiments. J Cerebral Blood Flow Metabolism. 1996;16, 7–22.

Kahkonen, S., Komssi, S., Wilenius, J., Ilmoniemi, R.J. Prefrontal TMS produces smaller EEG responses than motor-cortex TMS: implications for rTMS treatment in depression. Psychopharmacology (Berlin). 2005;181, 16-20.

Kopecek, M., Storkova, P., Kozeny J.,, Preiss M., Novak, T., Dockery, C., Horacek, J. Influence of cerebellar rTMS to verbal fluency – pilot study. Psychiatrie. 2004; 8 (Suppl.3), 52-56.

Kubicki, S., Herrmann, W.M., Fichte, K., Freund, G. Reflections on the topics: EEG frequency bands and regulation of vigilance. Pharmacopsychiatry 1979; 12, 237-245.

Miall, R.C., Christensen, L.O. The effect of rTMS over the cerebellum in normal human volunteers on peg-board movement performance. Neuroscience Letters 2004; 23;371,185-9.

Middleton, F., Strick, P. Cerebral Projections to the Prefrontal Cortex of the Primate. J Neuroscience 2001;21, 700-712.

Oldfield RC The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971 9:97-113.

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. Neuroscience Letters 2005;376, 188-93.

Pascual-Marqui, R.D., Michel, C.M., Lehmann, D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. International Journal of Psychophysiology 1994;18, 49-65.

Pascual-Marqui, R.D. Review of methods for solving the EEG inverse problem. International Journal of Bioelectromagnetism 1999;1, 75-86.

Pascual-Marqui, R.D. Standardized low resolution brain electromagnetic tomography (sLORETA): technical details. Methods & Findings in Experimental & Clinical Pharmacology. 2002;24, 5-12.

Post, A., Keck, M.E. Transcranial magnetic stimulation as a therapeutic tool in psychiatry: what do we know about the neurobiological mechanisms? J. Psychiatry Research 2001; 35, 193-215.

Pridmore, S., Fernandes, Filho J.A., Nahas, Z., Liberatos, C., George, M.S. Motor threshold in transcranial magnetic stimulation: a comparison of a neurophysiological method and a visualization of movement method. J ECT. 1998;14,:25-7.

Rapoport, M. The Cerebellum in Psychiatric Disorders. International Review of Psychiatry 2001;13, 295–301.

Schmahmann, J.D., Sherman, J.C. The cerebellar cognitive affective syndrome. Brain 1998;121, 561-79.

Schutter, D., van Honk, J., d'Alfonso, A., Peper, J., Panksepp, J. High frequency repetitive transcranial magnetic over the medial cerebellum induces a shift in the prefrontal electroencephalography gamma spectrum: a pilot study in humans, Neuroscience Letters 2003;336, 73-76.

Schutter DJ, van Honk J, d'Alfonso AA, Postma A, de Haan EH. Effects of slow rTMS at the right dorsolateral prefrontal cortex on EEG asymmetry and mood. Neuroreport. 2001;12(3):445-7.

Schlosser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimaki, A., Stevenson, J., Dewey S.L., Brodie J.D. Functional magnetic resonance imaging of human brain activity in a verbal fluency task. J Neurol Neurosurg Psychiatry 1998;64, 492-8.

Ugawa, Y., Uesaka, Y., Terao, Y., Hanajima, R., Kanazawa, I. Magnetic stimulation over the cerebellum in humans. Ann Neurology 1995;37, 703-713.

Wassermann, E.M., Grafman, J., Berry, C., Hollnagel, C., Wild K., Clark K., Hallet M. Use and safety of a new repetitive transcranial magnetic stimulator. Electroencephalography Clinical Neurophysiology 1996;101, 412-417.

Werhahn KJ, Taylor J, Ridding M, Meyer BU, Rothwell JC. Effect of transcranial magnetic stimulation over the cerebellum on the excitability of human motor cortex. Electroencephalogr Clin Neurophysiol. 1996;101(1):58-66.