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Low Frequency repetitive Transcranial Magnetic Stimulation: Potential role in treatment of patients with hemispheric cerebellar strokes

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Case report

Five years prior to TMS study, a 64 years old left-handed man with mild tremor-predominant Parkinson's disease that predominantly affected his right side experienced a large embolic left cerebellar infarct and subsequently required cerebellar hemispherectomy due to complications of cerebellar edema. He had no other evidence of brain lesions or stroke (Supplementary Figure). Patient was on Parkinson's medication Carbidopa/Levodopa 25–100mg 3 times per day and denied having ON of OFF periods. Residual difficulties with coordination, speech, fine motor movements, spasticity and most prominently his balance led to the permanent use of a wheel chair and required constant help from a caregiver. Other deficits include difficulties with handwriting, cutting food, scanning speech, turning in bed, and some numbness over his right side. Low Frequency (1Hz) repetitive Transcranial Stimulation (rTMS) was delivered onto the intact cerebellar hemisphere for two consecutive weeks and underwent pre- and post-TMS fine and gross motor assessments as well as cognitive testing (see supplementary methods for details).

Results

Subjective improvements

Our patient reported post-TMS sensory improvements on the affected side including sensation of touch on the right side of his face and torso as well as on the bottom of his right foot. The caregiver also reported easier transfers from and to wheelchair and some improvement in scanning speech which was also noted by our neurologist (BMK).

Quantitative assessment of physical and motor function

The subject was able to complete the Finger-Thumb Opposition task slowly and reaching fingernails instead of fingertips. Before TMS intervention, 9 and 15 appositions were executed with his left and right hand respectively. After 2 weeks of TMS, those numbers increased to 12 and 17 respectively (Fig. 1) suggesting an improvement in fine motor skills. When gross motor skills were assessed, neither the Rivermead Mobility Index (RMI), nor the stroke Rehabilitation Assessment of Movement (STREAM) or the Tinetti test showed any improvement (Fig. 1) with respective scores of 2/15, 3/56 and 1/28. However, the patient did demonstrate a slight increase in functional mobility independence for sit to stand, sitting balance, and bed mobility (summarized in Supplementary Table). Similarly, TMS sessions were beneficial to trunk control, as the Trunk Control Test for Motor Impairment After Stroke went from 37/100 to 49/100 after TMS. Specifically, the patient demonstrated improved scores for sitting balance edge of bed from 12 to 25, which demonstrates improved trunk control (Fig. 1).

Quantitative assessment of cognitive function

Due to motor control issues with his hands, the subject was unable to complete the written part of the MoCA test. TMS intervention did not affect any of the scores relative to picture naming, attention, memory and orientation. However, after 2-weeks TMS stimulation, language skills were improved and total MoCA score changes from 19/30 to 21/30, with improvement in verbal fluency and recall.

Discussion and conclusion

We report motor and cognitive improvements following 14 days of low-frequency cerebellar rTMS in a patient 5-years post-cerebellar infarct and hemispherectomy. Our results extend recent findings using rTMS for cerebellar ataxia [1] and stroke [2]. This is the first study targeting the spared hemisphere to investigate potential compensatory therapy in a patient with complete absence of lesioned cerebellar hemisphere. While cerebellar control of motor functions is mostly ipsilateral, bilateral activation is commonly observed [3]. Stimulation of the spared cerebellar hemisphere thus might have partly restored the neurophysiological homeostasis ipsi- and contra-lateral to the lesion due to the loss of the left hemisphere. This would explain the reported mild improvements, especially the improvement in touch sensation, which has previously been linked to functional brain changes in stroke patients [4].

We demonstrated rTMS-related improvements in the Trunk Control Test, specifically in the area of seated balance, suggesting that low-frequency cerebellar rTMS therapy could have improved cerebello-cerebral connections involved in mobility and balance, as described previously in patients with spinocerebellar degeneration [5]. Balance control also relies on functional neuronal circuits

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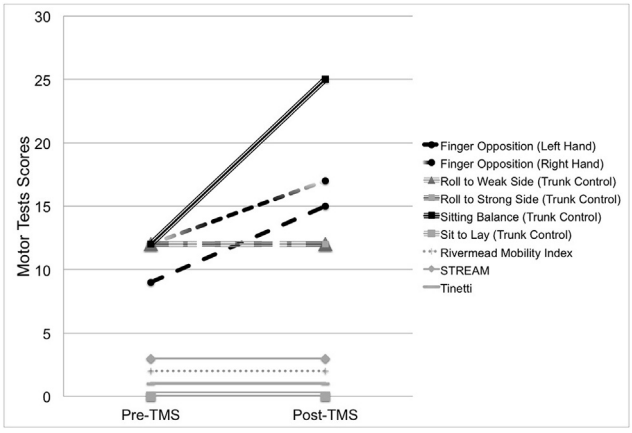

Fig. 1. Motor Control and Physical Mobility Tests: Scores improved after rTMS intervention in both affected and non-affected sides for the Finger Opposition Test and for the Sitting Balance Portion of Trunk Motor Control Impairment after Stroke Scale (in black color). No other change was found on other gross motor assessments (in gray color).

originating from the flocculonodular lobe of the cerebellum (or vestibulocerebellum [6]). It is unclear whether this area has suffered from the stroke, but it is possible that vestibulocerebellar Purkinje neurons were affected by rTMS.

We finally reported some post-TMS changes on language, specifically verbal fluency and recall, in contrast to another study using cerebellar stimulation [7]. Beside its role in motor coordination, the cerebellum, particularly the right side, is reliably activated during language paradigms such word/letter generation and verbal fluency tasks [8]. It has been shown that different current directions may significantly affect the results [9] so it is possible that we targeted different neuronal populations than the aforementioned studies or that there were ceiling effects with stimulation in healthy populations.

In this case study, we provide further evidence for the efficacy of cerebellar stimulation as a treatment strategy in cerebellar stroke. While it is possible that some of this patient's improvements may be related to changes in his Parkinson's disease (PD) as has been reported with cerebellar TMS [10,11], we feel that it is more likely that improvements were related to cerebellar effects as he had mild PD and his scanning speech, severe ataxia and other disabling symptoms arose at the time of the stroke and are more consistent with cerebellar injury. With a lack of both control subjects and control conditions, future controlled trials are warranted to further explore the effects of TMS therapy in those vulnerable patients.

Consent

This study was approved by the Colorado Multiple Institutional Review Board (COMIRB) and written informed consent was obtained by the patient for the case report and images to be published.

Relevant conflicts of interests

Nothing to report.

Financial disclosures for the previous 12 months

Isabelle Buard received a research grant from University of Colorado Movement Disorders Center.

Jean Berliner does not have anything to disclose.

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Authors' contributions

Conceived and designed the experiments, IB BK. Performed the experiments, IB JB. Analyzed the data, IB JB. Wrote the paper, IB JB. Reviewed and revised the manuscript and approved the final manuscript as submitted, IB JB and BK.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.brs.2018.02.012.

References

[1] Farzan F, Wu Y, Manor B, Anastasio EM, Lough M, Novak V, Greenstein PE, Pascual-Leone A. Cerebellar TMS in treatment of a patient with cerebellar ataxia: evidence from clinical, biomechanics and neurophysiological assessments. Cerebellum 2013;12:707–12.
[2] 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;46:418–23.
[3] Grodd W, Hulsmann E, Lotze M, Wildgruber D, Erb M. Sensorimotor mapping of the human cerebellum: fMRI evidence of somatotopic organization. Hum Brain Mapp 2001;13:55–73.
[4] Bannister LC, Crewther SG, Gavrilescu M, Carey LM. Improvement in touch sensation after stroke is associated with resting functional connectivity changes. Front Neurol 2015;6:165.
[5] Shiga Y, Tsuda T, Itoyama Y, Shimizu H, Miyazawa KI, Jin K, Yamazaki T. Transcranial magnetic stimulation alleviates truncal ataxia in spinocerebellar degeneration. J Neurol Neurosurg Psychiatr 2002;72:124–6.
[6] Schoch B, Hogan A, Gizewski ER, Timmann D, Konczak J. Balance control in sitting and standing in children and young adults with benign cerebellar tumors. Cerebellum 2010;9:324–35.
[7] Arasanz CP, Staines WR, Roy EA, Schweizer TA. The cerebellum and its role in word generation: a cTBS study. Cortex J Devoted Study Nervous Syst Behavior 2012;48:718–24.
[8] Frings M, Dimitrova A, Schorn CF, Elles HG, Hein-Kropp C, Gizewski ER, Diener HC, Timmann D. Cerebellar involvement in verb generation: an fMRI study. Neurosci Lett 2006;409:19–23.
[9] Brasil-Neto JP, Cohen LG, Panizza M, Nilsson J, Roth BJ, Hallett M. Optimal focal transcranial magnetic activation of the human motor cortex: effects of coil orientation, shape of the induced current pulse, and stimulus intensity. J Clin Neurophysiol: Offic Publ Am Electroencephalographic Soc 1992;9:132–6.
[10] Minks E, Marecek R, Pavlik T, Ovesna P, Bares M. Is the cerebellum a potential target for stimulation in Parkinson's disease? Results of 1-Hz rTMS on upper limb motor tasks. Cerebellum 2011;10:804–11.
[11] Koch G, Brusa L, Carrillo F, Lo Gerfo E, Torriero S, Oliveri M, Mir P, Caltagirone C, Stanzione P. Cerebellar magnetic stimulation decreases levodopa-induced dyskinesias in Parkinson disease. Neurology 2009;73:113–9.

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