Magnetic stimulation of the cerebellum. Moving towards the clinic

Dear Reader,

Transcranial magnetic stimulation (TMS) is a brain stimulation technique that is attracting growing interest due to its potential for intervention in various neurological and psychiatric conditions. The TMS principle is simple: by generating a controlled magnetic field at high intensity, TMS can induce a local current flow in brain tissue thereby modifying local microcircuit excitability (Hallett et al., 2006). On the one hand, TMS can be used to probe the brain activity relevant to the execution of sensorimotor and cognitive tasks with millisecond precision (Hallett et al., 2006), on the other, when applied repeatedly (repetitive TMS, rTMS), it can be used to promote mechanisms of long-term synaptic plasticity (Huang et al., 2005). This potential for long-lasting modifications of cortical excitability has been translated into clinical practice. For example, rTMS has been applied over the prefrontal cortex to modify the course of depression (George et al., 2013) and over the parietal cortex to accelerate functional recovery following ischemic stroke (Koch et al., 2012). Within the same framework. TMS has recently been applied to the cerebellum in order to investigate the contribution of cerebellothalamo-cortical circuits in several motor and cognitive tasks (Grimaldi et al., 2014) and to investigate the possibility that non-invasive modulation of these networks could be useful to treat specific neurological symptoms (Koch, 2010). In this issue of Functional Neurology, Bonnì and colleagues applied a two-week course of intermittent theta burst stimulation, a form of rTMS, over the lateral cerebellum in a sample of patients with ataxia due to chronic posterior circulation ischemic stroke. The hypothesis was that cerebellar rTMS, by promoting mechanisms of cerebellar plasticity, might be effective in improving some motor functions, and that this would occur as a result of increases in the activity of neural circuits originating from the cerebellar cortex, due to remodeling of the long-distance connections with the thalamus and the contralateral motor cortex. In these patients, cerebellar rTMS improved symptoms of gait and posture disturbances. This clinical improvement was paralleled by changes in the excitability of the contralateral motor cortex with an increase in intracortical facilitation. This study is relevant since it provides additional evidence that longlasting modification of cerebellar activity may have some persistent clinical effects, at least in the motor domain (Koch et al., 2009). Although potentially interesting, the study in question was performed in a small sample of patients and needs to be replicated in larger placebo-controlled clinical trials. Moreover, future studies using a multimodal approach

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combing TMS with functional MRI and EEG would allow a better understanding of how the modulation of cerebellar

synaptic functions may remodel long-distance interconnected networks (Grefkes and Fink, 2011).

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References

Bonnì S, Ponzo V, Caltagirone C, et al (2014). Cerebellar theta burst stimulation in stroke patients with ataxia. Funct Neurol Apr 7:1-5. [Epub ahead of print]

George MS, Taylor JJ, Short EB (2013). The expanding evidence base for rTMS treatment of depression. Curr Opin Psychiatry 26: 13-18. Grefkes C, Fink GR (2011). Reorganization of cerebral networks after stroke: new insights from neuroimaging with connectivity approaches. Brain 134: 1264-1276.

Grimadi G, Argyropoulos GP, Boehringer A, et al (2014). Non-invasive cerebellar stimulation--a consensus paper. Cerebellum 13:121-138. Hallett M (2007). Transcranial magnetic stimulation: a primer. Neuron 55:187-199.

Huang YZ, Edwards MJ, Rounis E, et al (2005). Theta burst stimulation of the human motor cortex. Neuron 45: 201-206.

Koch G (2010). Repetitive transcranial magnetic stimulation: a tool for human cerebellar plasticity. Funct Neurol 25: 159-163.

Koch G, Bonnì S, Giacobbe V, et al (2012). θ-burst stimulation of the left hemisphere accelerates recovery of hemispatial neglect. Neurology 78: 24-30.

Koch G, Brusa L, Carrillo F et al (2009). Cerebellar magnetic stimulation decreases levodopa-induced dyskinesias in Parkinson disease. Neurology 73 :113-119.