LETTER TO THE EDITOR

Reply: A single session of cerebellar theta burst stimulation does not alter writing performance in writer’s cramp

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Sir,

In their Letter to the Editor, Linssen et al. (2014) report the failure of a single session of continuous theta burst transcranial magnetic stimulation (TBS) of posterior cerebellum to improve the writing performance of patients with writer’s cramp. The authors state that they derived the rationale for their study from the conclusions of our study entitled ‘Defective cerebellar control of cortical plasticity in writer’s cramp’ published in Brain (Hubsch et al., 2013). We would like to emphasize that our study showed that, in patients with writer’s cramp, TBS of the posterior cerebellar cortex, be it excitatory (intermittent TBS) or inhibitory (continuous TBS), failed to modulate the plastic responsiveness of the hand representation in the primary motor cortex (M1), to paired associative stimulation. This was in sharp contrast with the results obtained in healthy controls, in whom cerebellar stimulation exerted a stimulation pattern-specific priming of the M1 responsiveness of the hand representation to plastic forces. The mechanism through which cerebellum exerts this priming effect on M1 was demonstrated by our group to be through the processing of sensory afferent input (Popa et al., 2013). Based on this, we reasoned that in writer’s cramp the cerebellum may not play its normal role of scaling the sensory information necessary for selecting and fine-tuning the motor commands. This may have resulted in an abnormal encoding of writing motor programs and eventually to abnormal writing performance when such motor programs are recalled. Accordingly, the cerebellar dysfunction leads to abnormal motor engrams for writing and does not interfere online with the writing movement per se. Therefore we do not expect one session of either type of cerebellar stimulation to be able to influence motor engrams stored for years or decades and improve the writing performance. In the literature, one session of non-invasive stimulation to the posterior cerebellum was shown to interfere with different types of ongoing motor learning: adaptive motor learning (Galea et al., 2011; Panouillères et al., 2012), associative motor learning (Hoffland et al., 2012), procedural motor learning (Torriero et al., 2004), practice-related learning (Li Voti et al., 2014), yet multiple sessions (at least 10 over 2 weeks) of bilateral cerebellar stimulation were necessary to influence aberrant motor engrams. Indeed, multiple bilateral sessions had a positive effect on levodopa-induced dyskinesia in Parkinson’s disease (Koch et al., 2009; Kishore et al., 2014) and a modest effect in...
cervical dystonia (Koch et al., 2014). So an important conclusion that emerges from the negative results found by Linssen et al. (2014) is that one single session of non-invasive cerebellar stimulation is insufficient to improve complex disorders like dystonia, a condition in which even invasive deep brain stimulation takes weeks to induce any significant improvement. Therefore, multiple days/weeks of cerebellar stimulation is definitely the way to proceed if we aim to provide significant clinical benefit to patients with dystonia.

Little is known about how the cerebellum participates in the computations of the motor cortex—the final output motor structure, in the frame of motor learning/adaptation—and this makes it difficult to predict the potential impact of one (and even multiple) session of continuous TBS to cerebellum on the writing performance. The complex link between the induction of plasticity in the cerebellar cortex as induced by cerebellar TBS and the way it modulates a subsequent plasticity in the sensorimotor cortex and motor performances was illustrated in our study (Hubsch et al., 2013). Even though as a group, patients with writer’s cramp displayed no cerebellar modulation of motor cortex plasticity, at an individual level, we found a correlation between the online adaptation to a pointing task with visuomotor conflict and some residual reactivity of the motor cortical plasticity to cerebellar continuous TBS. Impaired online adaptation was seen in those with preserved response to continuous TBS to cerebellum. There is no obvious explanation for such a negative correlation. One possibility would be that a compensatory hyperactive cerebellum might be refractory to stimulation due to a ceiling effect, yet allows better performance. In any case, this does not provide a strong hypothesis to test for therapeutic response to a single session of continuous TBS to the cerebellum.

References