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Research report

The effect of the anodal transcranial direct current stimulation over the cerebellum on the motor cortex excitability

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ABSTRACT

This study was designed to investigate whether the cerebellum has an inhibitory effect on motor cortical excitability.

Sixteen healthy adults (age range, 25–50 years, five female) participated in the study. Anodal cerebellar transcranial direct current stimulation (a-cTDCS) was used to modulate cerebellar excitability. A-cTDCS was given for 20 min at 1 mA intensity. The automatic threshold tracking method was used to investigate cortical excitability. Resting motor threshold (RMT), short interval intracortical inhibition (SICI), short interval intracortical facilitation (SICF), intracortical facilitation (ICF), and the input output curve (I-O curve) were motor cortical excitability parameters.

a-cTDCS caused a reduction in overall SICI and the reduced SICF for interstimulus intervals (ISIs) to 2.4–4.4 ms. a-cTDCS has no effect on ICF, RMT, and the I-O curve. There were no significant changes in any of these cortical excitability parameters after sham cTDCS.

Results of the study indicate that a-cTDCS has a dual (both inhibitory and excitatory) effect on motor cortical excitability, rather than a simple inhibitory effect. The cerebellum modulates both the inhibitory and facilitatory activities of motor cortex (M1) and suggest that cerebello–cerebral motor connectivity is more complex than solely inhibitory or facilitatory connections.

1. Introduction

The cerebellum plays an important role in the regulation and modulation of motor control. It has connections with the premotor, prefrontal, and parietal areas and motor cortex (Caligiore et al., 2017). One of the main connections between the cerebellum and M1 is the cerebello–thalamo–cortical pathway. The dentate nucleus of the cerebellum sends projections to the ventral lateral nucleus of the thalamus, forming the dentato–thalamo–cortical pathway (Kerry and Strick, 2003). Fibers from the ventral thalamus send excitatory inputs to M1. The main output neurons of the cerebellum, Purkinje cells, form inhibitory synapses with deep cerebellar nuclei. Thus, the activation of Purkinje cells inhibits the excitatory effect of the cerebellum on M1 via the dentato–thalamo–cortical pathway.

Transcranial magnetic stimulation (TMS) permits the non-invasive evaluation of cerebellar–cortical connections. Ugawa et al. demonstrated that magnetic stimulation of the cerebellum 5–7 ms before magnetic stimulation of M1 resulted in reduced motor-evoked potential (MEP) amplitudes, indicating the inhibition of M1 excitability (Ugawa et al., 1995). The basic mechanism of this phenomenon, termed cerebellar brain inhibition, is thought to consist of the activation of Purkinje cells via cerebellar TMS resulting in reduced exitatory input to M1 (Ugawa et al., 1995, 1997). The cerebellum modulates intracortical motor inhibition and facilitation in healthy individuals, which can be evaluated using TMS (Oliveri et al., 2005; Fierro et al., 2007; Koch et al., 2008; Langguth et al., 2008; Galea et al., 2009; Naro et al., 2016). However, the results of studies on the effect of the cerebellum on M1 excitability and connectivity are inconsistent, and the magnitudes of the effect observed vary (Tremblay et al., 2016).

cTDCS is reasonably a new, non-invasive method of cerebellar stimulation used to study functional and physiologic aspects of the cerebellum (Priori et al., 2014). It changes the excitability of the cerebellar cortex depending on the stimulation polarity (Ferrucci et al., 2015).

The aim of this study was to elucidate the effect of the cerebellum on M1 excitability and connectivity in more detail. To achieve this, we used threshold-tracking method to investigate M1 excitability and connectivity. We used cTDCS to modulate cerebellar excitability, hypothesizing that anodal cTDCS would increase cerebellar excitability

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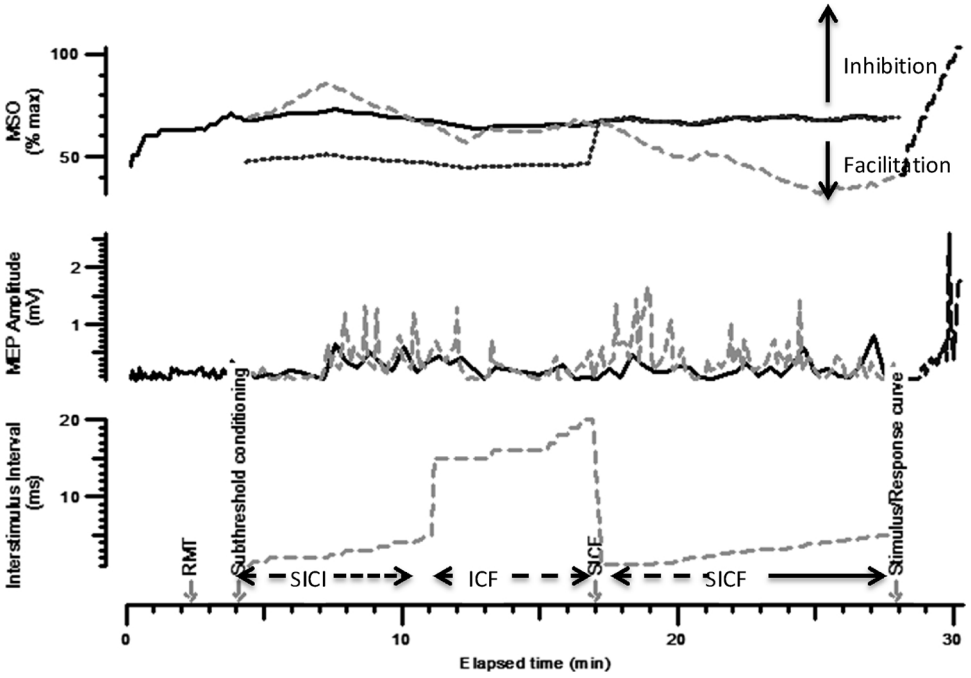

Fig. 1. Upper trace: Four channel recording. Channel 1 (solid line) tracks test stimulus (RMT) response, channel 2 (short dashed line) tracks subtreshold (70% RMT) stimulus response, channel 3 (long dashed line) tracks conditioned (test stimulus and subtreshold stimulus with different ISIs) stimulus response. Note that on the subtreshod conditioning stimulus paradigm, conditioned stimulus (channel 3) MSO values higher than test stimulus (channel 1) that indicates intracortical inhibition during ISIs of SICI (1–4 ms) while it reduces below to channel 1 values during ISIs of ICF (15–20 ms). On the SICF paradigm, channel 2 tracks threshold (RMT) response as channel 1. Channel 3 consists two equal test stimulation ISIs between 1 and 5 ms with 0.2 ms step. As seen in the trace facilitation (reduced channel 3 MSO than channel 1) occurs during this period. Channel 4 (folded line) designed for I-O curve paradigm. Middle trace: the system automatically tracks peak-to-peak MEP amplitudes for each TMS. If the MEP amplitude fails below acceptable values (−25% of 200 μV), the system automatically increases the magnetic stimulator output and vice versa to achieve acceptable values In this way, the system aimed to sustain target MEP response during whole recording period. Lower trace indicates ISIs of the conditioned stimulus (channel 3)..

and, in accordance with the observations of Galea et al. (Galea et al., 2009), that activation of Purkinje cells in the cerebellar cortex by anodal cTDCS would decrease motor-cortical excitability via suppression of the dentato–thalamo–cortical pathway.

2. Methods

2.1. Participants

Sixteen healthy adults (age range: 25–50 years, five female) participated in this study. All participants were right-handed without any neurologic or musculoskeletal disorders affecting the upper limbs. All participants were informed about the process and provided written consent to participate. A local ethics committee approved for this study.

2.2. Motor-cortical stimulation

The M1 was stimulated with a figure-of-eight-shaped coil 9 cm in diameter connected to two Magstim 200 stimulators linked with a Bistim module. (Bistim, Magstim Co. Ltd). The coil was held tangentially on the scalp and orientated 45^0 to the midline to induce a postero–anterior electromagnetic field in M1.

2.3. Modulation of the cerebellum

cTDCS was delivered via two sponges soaked in saline solution. The active electrode was 5 × 5 cm (current density: 0.08 mA/cm^2), whereas the reference electrode was 9 × 5 cm (current density: 0.044 mA/cm^2). The active electrode was placed on the right cerebellar cortex 3 cm lateral to the inion, whereas the reference electrode was positioned on the right buccinator muscle. Two different stimulation modalities, anodal and sham, were used. Anodal stimulation was given for 20 min at an intensity of 1 mA. Sham cTDCS was delivered in an identical manner, however, the current intensity was decreased to 0 mA after 30 s. The M1 excitability study protocol was performed before and immediately after cTDCS in both anodal and sham cTDCS sessions.

2.4. Electromyography recording

Electromyography (EMG) recordings were made from the right first dorsal interosseous muscle using surface recording electrodes and the belly-tendon method. The analog signal was amplified (1 mV/V) and filtered (3 Hz–10 kHz) using a Dantec™ Cantata EMG machine (Dantec Dynamics A/S, Skovlunde, Denmark). The signal was sampled at 10 kHz using a 16-bit data-acquisition card (USB 6221, National Instruments Corp., Austin, Texas, USA). Data acquisition and magnetic stimulus output were controlled by QTRAC software (© Professor Hugh Bostock, Institute of Neurology, Queen Square, London, UK). All EMG recordings were performed with the participant in a sitting position and at rest.

2.5. Evaluation of motor-cortical excitability and connectivity using the automatic threshold-tracking method

During the threshold-tracking analysis of M1 excitability and connectivity, changes in magnetic stimulator output were monitored instead of variations in MEP amplitude. The RMT was defined as the minimum magnetic stimulus intensity required to produce an MEP amplitude of 200 μV, and was automatically checked during the whole process. The findings of Fisher et al. demonstrated that a MEP amplitude of 200 μV represents the middle of the linear relationship between the logarithm of the MEP amplitude and the stimulus (Fisher et al., 2002). If the MEP amplitude fails below acceptable values (−25% of 200 μV), the system automatically increases the magnetic stimulator output and vice versa to achieve acceptable values. Four-channel recording was used as follows: Channel 1 recorded and tracked test-stimulus intensity to obtain the target MEP response (RMT), Channel 2 was a conditional stimulus channel set to subthreshold magnetic stimulus intensity (70% RMT) for the SICI and ICF paradigms or to threshold intensity (equal to Channel 1/the RMT) for the SICF paradigm, in Channel 3, both the test and conditional stimuli were given at different intervals depending on the study paradigm, and Channel 4 was designed for the input–output (I–O) curve paradigm (Fig. 1).

The following M1 excitability and connectivity parameters were studied: