Abstract

Background: Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique able to transiently modulate brain activity, is surging as one of the most promising therapeutic solutions in many neurological and psychiatric disorders. However, profound limitations exist in current placebo (sham) protocols that limit single- and double-blinding, especially in non-naïve subjects.

Objective: To ensure better blinding and strengthen reliability of tDCS studies and trials, we tested a new optimization algorithm aimed at creating an "active" sham tDCS condition (*ActiSham* hereafter) capable of inducing the same scalp sensations perceived during real stimulation while preventing currents from reaching the cortex and cause changes in brain excitability.

Methods: A novel model-based multielectrode technique — optimizing the location and currents of a set of small electrodes placed on the scalp — was used to control the relative amount of current delivered transcranially in real and placebo multichannel tDCS conditions. The presence, intensity and localization of scalp sensations during tDCS was evaluated by means of a specifically designed questionnaire administered to the participants. We compared blinding ratings by directly addressing subjects' ability to discriminate across conditions for both traditional (Bifocal-tDCS and Sham, using sponge electrodes) and our novel multifocal approach (both real Multifocal-tDCS and ActiSham). Changes in corticospinal excitability were monitored based on Motor Evoked Potentials (MEPs) recorded via concurrent Transcranial Magnetic Stimulation (TMS) and electromyography (EMG).

Results: Participants perceived Multifocal-tDCS and ActiSham similarly in terms of both localization and intensity of scalp sensations, whereas traditional Bifocal stimulation was rated as more painful and annoying compared to its Sham counterpart. Additionally, differences in scalp localization were reported for active/sham Bifocal-tDCS, with Sham tDCS inducing more widespread itching and burning sensations. As for MEPs amplitude, a main effect of stimulation was found when comparing Bifocal-Sham and ActiSham ($F_{(1,13)} = 6.67$, $p = .023$), with higher MEPs amplitudes after the application of Bifocal-Sham.

Conclusions: Compared to traditional Bifocal-tDCS, ActiSham offers better participants' blinding by inducing very similar scalp sensations to those of real Multifocal tDCS both in terms of intensity and localization, while not affecting corticospinal excitability.