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Research report

Transcranial direct current stimulation over the supplementary motor area modulates the preparatory activation level in the human motor system

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HIGHLIGHTS

- Voluntary reaction time was examined following offline tDCS of SMA.
- A loud, startling acoustic stimulus was used as a secondary index of preparation.
- Anodal tDCS resulted in significantly faster reaction times.
- Cathodal tDCS led to slowed reactions and decreased response triggering by startle.

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ABSTRACT

Transcranial direct current stimulation (tDCS) is a non-invasive stimulation method that can induce transient polarity-specific neuroplastic changes in cortical excitability lasting up to 1 h post-stimulation. While excitability changes with stimulation over the primary motor cortex have been well documented, the functional effects of stimulation over premotor regions are less well understood. In the present experiment, we tested how cathodal and anodal tDCS applied over the region of the supplementary motor area (SMA) affected preparation and initiation of a voluntary movement. Participants performed a simple reaction time (RT) task requiring a targeted wrist-extension in response to a go-signal. In 20% of RT trials a startling acoustic stimulus (SAS) was presented 500 ms prior to the "go" signal in order to probe the state of motor preparation. Following the application of cathodal, anodal, or sham tDCS (separate days) over SMA for 10 min, participants performed blocks of RT trials at 10 min intervals. While sham stimulation did not affect RT or incidence of early release by the SAS, cathodal tDCS led to a significant slowing of RT that peaked 10 min after the end of stimulation and was associated with a marked decrease in the incidence of movement release by the SAS. In contrast, anodal tDCS resulted in faster RTs, but the incidence of release was unchanged. These results are consistent with the SMA playing a role in the pre-planning of movements and that modulating its activity with tDCS can lead to polarity-specific changes in motor behavior.

1. Introduction

The supplementary motor area (SMA) has long been known to play a role in the control of movement [1], particularly in the advance preparation and initiation of voluntary actions [2]. Experiments in non-human primates have provided evidence that the SMA contains a large proportion of movement-related neurons that are active throughout the preparatory time interval and demonstrate a gradual increase in firing rate that peaks near the onset of movement [3–5]. Similarly, scalp surface EEG and subdural electrocortigography (ECoG) studies in humans have shown that self-initiated movements are preceded by a slow rising movement-related potential over the region of the SMA that begins as much as 3 s prior to movement [6–9]. SMA neurons have also been shown to be preferentially active prior to self-paced, self-initiated movements, yet SMA activity is also seen during some forms of externally cued movements, such as instructed-delay tasks [8,10]. These

Non-standard abbreviations: ECR, extensor carpi radialis longus; FCR, flexor carpi radialis; RT, reaction time.

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findings demonstrate the generalized role of the SMA in the early preparation of voluntary actions.

The SMA may also contribute to the initiation of movement. This idea is based on evidence that many SMA neurons show activity that is time-locked to the onset of muscle activity [11,12]: electrical stimulation of the SMA evokes a complex pattern of motor output [1,13–15], and lesions of the SMA are associated with a transient akinetic state [16–18], including deficits in gait initiation and execution [19].

Despite the consensus that the SMA is involved in movement preparation and initiation, the role the SMA plays in contributing to preparatory motor set, organizing of the spatial and temporal parameters of motor output, and the release of action is unclear [20]. Non-invasive brain stimulation methods can be used to alter the excitability of underlying cortical areas, and thus provides the means to probe the effects of stimulation on motor behavior. However, the results of studies using transcranial magnetic stimulation (TMS) have been equivocal. For example, early and late single-pulse transcranial magnetic stimulation (TMS) applied over SMA did not affect either reaction time (RT) or movement time in healthy humans [21,22]; while on the other hand, repetitive TMS has been shown to either improve [23] or degrade [24] motor performance in patients with Parkinson's disease. Another means of modulating cortical excitability is through the use of transcranial direct current stimulation (tDCS). By applying small amount of direct current (e.g. .5–1 mA) over a cortical area of interest for a short period of time using scalp surface electrodes, tDCS has been shown to modulate cortical excitability in humans (for reviews see [25,26]). For instance, anodal stimulation applied over primary motor cortex (M1) has been shown to increase TMS-induced motor evoked potential amplitudes elicited from the site of tDCS stimulation for up to 90 min post-stimulation [27]. Conversely, decreased M1 excitability has been demonstrated using cathodal stimulation [26]. If the excitability of SMA plays a role in the preparatory state of the motor system, then anodal tDCS and cathodal tDCS applied over SMA should lead to increases or decreases, respectively, in the level of motor preparation.

In order to assess the extent and the timing of early motor preparation achieved, instructed-delay RT task paradigms can be used, as they provide precise control of the time interval between a warning ("get ready") and imperative ("go") stimulus. When there is some unpredictability about the timing between the warning and imperative stimulus, motor preparation can be indexed with RT, where faster RTs are associated with a greater level of advance preparatory activity (e.g., [28,29]). Additionally, the state of preparation of the intended movement during the delay interval can also be probed by delivering a startling acoustic stimulus (SAS) prior to, or in place of, the imperative cue. Under simple RT conditions, the SAS evokes an early and rapid release of the planned movement if it is sufficiently prepared ([30–32], for reviews see [33,34]).

Thus the current study aimed to investigate the functional effect of modulating SMA activity using tDCS. Specifically, we hypothesized that anodal stimulation of the SMA would lead to an increased state of motor preparation as evidenced by decreased RTs and an increase in the proportion of trials in which the SAS evoked the early release of movement. In contrast, we hypothesized that cathodal stimulation would result in increased RTs and a decrease in the proportion of movements triggered by SAS.

2. Methods

2.1. Participants

Ten healthy volunteers (8 M, 2F; 30.3 ± 10.0 years) participated in the active tDCS experiments which were completed in two separate sessions, each session corresponding to a different stimulation polarity (see Section 2.3). In addition, seven healthy volunteers (3 M, 4F; 27.0 ± 7.3 years) participated in a single sham tDCS testing session. All participants gave written informed consent, and the study was conducted in accordance with the ethical approval of the Institutional Research Board at Northwestern University, and the Research Ethics Board at the University of Ottawa, and conformed to the latest revision of the Declaration of Helsinki at the time of testing.

2.2. Task and feedback

Participants sat in a chair facing a computer monitor and gripped a handle attached to the arm of a custom wrist manipulandum that allowed measurement of wrist angular displacement. Participants performed a 20 degree right wrist extension from a home position of 10 degrees of flexion to a fixed target as quickly and accurately as possible upon the presentation of a visual "go" signal (appearance of a green square on the computer screen). The go signal occurred 2–3 s (variable) following a warning signal. Final position feedback was provided in between trials by representing the position of the manipulandum with a 1 cm tall yellow cursor line within a horizontal (1 cm × 15 cm) black rectangle presented on the computer screen with respect to a blue vertical cursor line that represented the target. Real time position feedback was only provided during practice. Further details of the experimental task and equipment have been published previously (see variable foreperiod condition, [31]). Practice trials were given prior to data collection to allow subjects to become familiar with the task and to remove learning effects [35,36]. Participants only required 10–25 practice trials to become proficient at the task. Wrist position feedback was given visually with a cursor that moved horizontally on the computer screen in direct relation to the manipulandum (for details see [31]). During testing, final position feedback was given approximately 1 s after each movement ended. In this way, knowledge of results was available, helping to stabilize movement accuracy performance.

Participants performed 7 blocks of 25 RT trials. Each block took approximately 4.5 min to complete. Two blocks were performed prior to tDCS, 1 block was performed immediately post-stimulation, and the remaining 4 blocks were initiated at 10 min intervals with respect to the end of stimulation. Participants sat quietly during the rest periods between testing blocks.

2.3. Transcranial direct current stimulation (tDCS)

Stimulation was delivered via two electrodes placed over the scalp. The "active" electrode was a sponge electrode (Empi Inc., Dupel B.L.U.E–medium butterfly 2.0 cm^3) measuring 8.1 cm^2 that was placed 1.8 cm anterior to the measured location of Cz (based on the international 10–20 system for EEG electrode placement). The active electrode was saturated with sterile saline (.9% NaCl) and was held in place if necessary using a standard EEG cap. The "return" electrode was a self-adhesive carbon–foam electrode (Empi Inc.) measuring 51 cm^2 (approx. 8.5 cm × 6 cm) that was placed centrally on the forehead directly above the eyebrows.

The placement location for the active electrode was determined using 2 methods: First, the scalp location immediately above the centroid of SMA was landmarked based on Talairach space mapped onto standardized head coordinates [37]. Second, in a subset of participants ($n = 5$) this location was confirmed using transcranial magnetic stimulation (TMS, Magstim Inc.) based on previous studies [22,38,39]. In short, TMS was delivered over the vertex and motor evoked potentials (MEPs) were recorded in tibialis anterior. The stimulating coil was then moved anteriorly in 5 mm increments and the location was noted where MEPs were no longer observed. In all cases the TMS-based localization ended up being ±2 mm from