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Revealing the brain's adaptability and the transcranial direct current stimulation facilitating effect in inhibitory control by multiscale entropy

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ABSTRACT

The abilities to inhibit impulses and withdraw certain responses are critical for human's survival in a fast-changing environment. These processes happen fast, in a complex manner, and sometimes are difficult to capture with fMRI or mean electrophysiological brain signal alone. Therefore, an alternative measure that can reveal the efficiency of the neural mechanism across multiple timescales is needed for the investigation of these brain functions. The present study employs a new approach to analyzing electroencephalography (EEG) signal: the multiscale entropy (MSE), which groups data points with different timescales to reveal any occurrence of repeated patterns, in order to theoretically quantify the complexity (indicating adaptability and efficiency) of neural systems during the process of inhibitory control. From this MSE perspective, EEG signals of successful stop trials are more complex and information rich than that of unsuccessful stop trials. We further applied transcranial direct current stimulation (tDCS), with anodal electrode over presupplementary motor area (preSMA), to test the relationship between behavioral modification with the complexity of EEG signals. We found that tDCS can further increase the EEG complexity of the frontal lobe. Furthermore, the MSE pattern was found to be different between high and low performers (divided by their stop-signal reaction time), where the high-performing group had higher complexity in smaller scales and less complexity in larger scales in comparison to the low-performing group. In addition, this between-group MSE difference was found to interact with the anodal tDCS, where the increase of MSE in low performers benefitted more from the anodal tDCS. Together, the current study demonstrates that participants who suffer from poor inhibitory control can efficiently improve their performance with 10 min of electrical stimulation, and such cognitive improvement can be effectively traced back to the complexity within the EEG signals via MSE analysis, thereby offering a theoretical basis for clinical intervention via tDCS for deficits in inhibitory control.

Introduction

Inhibitory control reflects the ability to suppress a prepotent response and is an important cognitive ability in almost every aspect of our daily life. It requires our brain to make a fast adaptation to an ever-changing environment. For example, when a driver is ready to step on the gas pedal to accelerate (the prepotent response to a green traffic light), the sudden appearance of a child running into the lane necessitates the driver to adapt to this fast environmental change and exercise strong inhibition to stop the initiated response. In the laboratory, inhibitory control is often investigated using a stop-signal task (Logan and Cowan, 1984; Logan and Irwin, 2000), where a 'go' signal requires a motor response from the participants, but an irregularly-intervening sudden 'stop' signal requires the response to be inhibited (e.g., Aron and Poldrack, 2006; Li et al., 2006, 2008; Swann et al., 2012). To quantify the performance on the stop-signal task, behavioral data have been modeled successfully as a race between the stop and go processes to obtain a measure for estimating the time needed to inhibit a response, referred to as the stop-signal reaction time (SSRT) (Logan and Cowan, 1984). Brain signals (e.g., BOLD signal, ECoG, and EEG) acquired from essential loci/electrodes during the stop signal task has also introduced some promising physiological measures that are related to behavioral performance (e.g., Li et al., 2006; Lo et al., 2013; Swann et al., 2009). However, beyond merely demonstrating a relationship between certain physiological measures and the behavioral performance, there is a need

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to investigate these brain signals using a measure that is able to theoretically quantify the adaptability and efficiency of neural systems during the processes of inhibitory control.

To better quantify the adaptability and efficiency of the neural signals during the stop-signal task, we calculated the multiscale entropy (MSE; Costa et al., 2002, 2005; Peng et al., 2009) of EEG signals acquired along with the stop-signal experiment. MSE, in short, is an extension of Shannon's entropy (Shannon and Weaver, 1949) and Pincus' approximate entropy (Pincus, 1991). The MSE calculates sample entropies (Richman and Moorman, 2000), a modification of approximate entropy, for biological signals by grouping data points with different timescales (coarse-grained time series). Sample entropy of each coarse-grained time series is a measure to reckon signal complexity by evaluating the occurrence of repetitive patterns. Therefore, low MSE signifies that the time series is more deterministic or regular, whereas high MSE indicates that the signal is more complex and information rich. Prior research has indicated that physical and mental illness are often related to decreased MSE in physiological signals (e.g., Catarino et al., 2011; Costa et al., 2005; Mizuno et al., 2010), whereas an increase of MSE in brain signals has been demonstrated as a critical index in development (McIntosh et al., 2008). Furthermore, previous studies have emphasized the MSE is vital to the understanding of brain mechanisms of cognition and behavior (Breakspear and McIntosh, 2011; Deco et al., 2011). Therefore, the current employment of MSE to understand inhibitory control is motivated by three basic hypotheses: 1) the complexity of a biological system reflects its ability to adapt and function in a fast-changing environment; 2) biological systems need to operate across multiple spatial and temporal scales, and hence their complexity is also multi-scaled; 3) the "ability to adapt" by the brain for a cognitive function is associated with the neuroplasticity of this function.

Based on such understanding of the MSE, the present study also applies anodal tDCS over the preSMA to facilitate the neuroplasticity of inhibitory control (Hsu et al., 2011; Liang and Juan, 2013; for other brain stimulation results that supported an essential role of preSMA in inhibitory control, please see Chen et al., 2009; Mars et al., 2009; Neubert et al., 2010; For a review see Neubert et al., 2012), thereby investigate how the MSE values change along with the facilitating effect of anodal tDCS. Anodal tDCS has been shown to be able to temporarily increase the firing rate of cortical neurons, thereby improving the neuroplasticity of the brain region where electricity was delivered (Bindman et al., 1964). By applying anodal tDCS over the preSMA, one study (Hsu et al., 2011) has demonstrated a robust improvement that can efficiently decrease the error rate in inhibitory control. Therefore, the current study aims to go beyond the original behavioral results and analyze any event-related or tDCS-induced complexity in electrophysiological signals behind inhibitory control. To this end, the aim of the current study is threefold: 1) to compare MSE of electrophysiological signals between successful and unsuccessful stop trials; 2) to see the changes in MSE after anodal tDCS application over preSMA; and 3) to identify the MSE pattern that is associated with superior performance in inhibitory control. We hypothesize that the electrophysiological signals from successful stop trials are more complex and information rich than those from unsuccessful stop trials. We also hypothesize that anodal tDCS over preSMA will increase the MSE and improve inhibitory control. In addition, we postulate that the MSE pattern of high-performing participants is different from that of low-performing participants, at least in some specific scales.

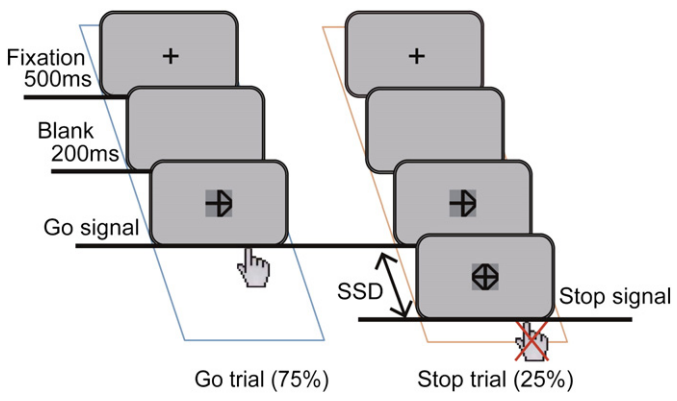

Fig. 1. Illustration of the stop-signal task.

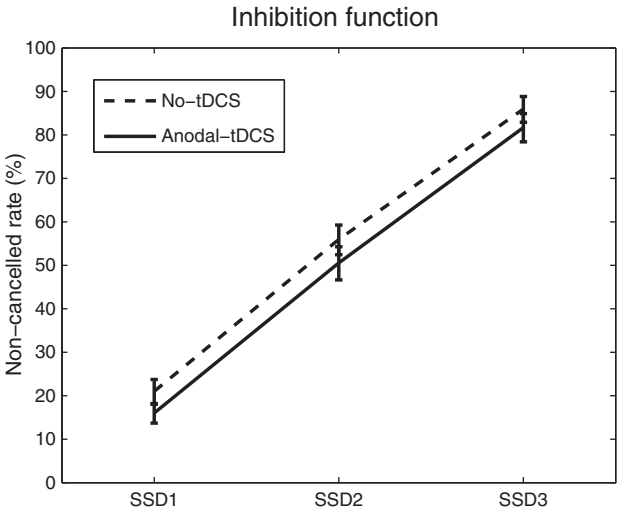

Fig. 2. Inhibition functions for each SSD. The non-cancelled rates of stop trials were reduced by anodal tDCS. Standard error of the mean (S.E.M.) at each SSD is indicated by the error bar.

Materials and methods

Eighteen neurologically normal adults (10 males, mean age = 25.4) participated in the experiment. Informed consent was obtained from each participant before the experiment. The experiment was approved by the Institutional Review Board of the Chang-Gung Memorial Hospital (Taoyuan, Taiwan).

Stop-signal paradigm

The stop-signal task consisted of two types of trials: *go*, which was signalled with an arrow, and *stop*, which was signalled with an arrow followed by a diamond (Fig. 1). In a go trial, each session began with a 500 ms central fixation cross, followed by a 200 ms blank screen. After the blank screen, an arrow (go signal) pointing either to the right or left was displayed, and participants were told to respond to the direction of the arrow with their corresponding index finger as soon as possible. Participants were also told that sometimes the arrow would be followed by a diamond (stop-signal) in the center of the display after a delay (stop-signal delay (SSD)), and that they should withhold their responses if the diamond appeared.

The experiment consisted of two formal sessions performed on two separate days: one with anodal tDCS over preSMA and the other with no tDCS to serve as a control condition. The two sessions were at least 24 h

Table 1
Behavior performance in inhibitory control.

	Anodal-tDCS	No-tDCS	*p* (*t*-test two-tailed)
Accuracy of go trials	97.16% (0.73%)	97.90% (0.36%)	0.3743
Mean RT of go trials (ms)	387.20 (6.99)	383.59 (5.72)	0.3813
Mean RT of USST (ms)	366.52 (7.12)	362.77 (5.82)	0.3499
SSRT (ms)	197.40 (3.37)	202.41 (3.85)	**0.0096****

Note: Standard errors are showed in brackets. ** indicates $p < 0.01$.