Delineating the effects of anodal transcranial direct current stimulation on myoelectric control based on slow cortical potentials

Anirban Dutta, Rahima S. Boulenouar, David Guiraud, and Michael A. Nitsche

Abstract— **Active cortical participation in rehabilitation procedures may be facilitated by modulating neuromuscular electrical stimulation (NMES) with electromyogram (EMG) and electroencephalogram (EEG) derived biopotentials, that represent simultaneous volitional effort. Here, the ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function, and connections is called neuroplasticity. Neuroplasticity is involved in post-stroke functional disturbances, but also in rehabilitation. Beneficial neuroplastic changes may be facilitated with an adjuvant treatment with non-invasive brain stimulation (NIBS). This paper presents the results from a motor cortex anodal tDCS-EEG/EMG study in healthy volunteers. We investigated slow cortical potentials (SCP) during self-initiated movements. In this preliminary study, we found that anodal tDCS increased baseline-normalized post-tDCS mean power in the Theta band (4-8Hz) of resting state EEG (60.71% vs. 8.36%; p<0.01), and decreased the slope of post-tDCS SCP from motor task-related EEG (-6.43 au/sec vs. -4.86au/sec; p=0.021) when compared to sham tDCS. These preliminary results are discussed based on an accumulator model for spontaneous neural activity which postulates that a decision threshold applied to auto-correlated noise—in this case the output of a leaky stochastic accumulator—can account for the specific shape of the SCP prior to movement. We postulate that the anodal tDCS facilitated change in the slope of SCP may be related to the reaction times during a cued movement task, since our prior work showed that anodal tDCS decreases the delay in initiation of muscle contraction and increases the delay in termination of muscle activity.**

I. Introduction

Stroke is caused when an artery carrying blood from heart to an area in the brain bursts or a clot obstructs the blood flow thereby preventing delivery of oxygen and nutrients. About half of the stroke survivors are left with some degree of disability. Innovative methodologies for restorative neurorehabilitation are urgently required to reduce long-term disability. The ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function and connections is called neuroplasticity. Neuroplasticity is involved in post-stroke functional disturbances, but also in rehabilitation. Beneficial neuroplastic changes may be facilitated with non-invasive electrotherapy, such as neuromuscular electrical stimulation (NMES) and non-invasive brain stimulation (NIBS). Active cortical participation in rehabilitation procedures may be facilitated by volitional control of NMES with electromyogram (EMG) and electroencephalogram (EEG) derived biopotentials, that represent simultaneous volitional effort. Moreover, NIBS techniques viz. transcranial direct current stimulation (tDCS) [1] may be used not only to facilitate motor learning [2] but also facilitate 'successful adaptation' towards long-term retention [3] [4] of volitionally controlled NMES. Here, Galea and coworkers [4] have dissociated the roles of the cerebellum and motor cortex (M1) during adaptive learning. Cerebellar excitability-enhancing anodal tDCS caused faster adaptation to the visuomotor transformation while M1 anodal tDCS did not affect adaptation, but resulted in a marked increase in retention. Our preliminary results from healthy subjects showed specific, and at least partially antagonistic effects, of M1 and cerebellar anodal tDCS on motor performance during cued myoelectric control [2]. The primary result was that offline cerebellar anodal tDCS increased the delay in initiation of cued EMG activity (quick initiation/termination of muscle activation i.e. 'ballistic EMG control') while M1 anodal tDCS decreased it, when compared to sham tDCS. However, online cerebellar anodal tDCS also decreased the learning rate during 'proportional EMG control' when compared to M1 anodal and sham tDCS which may be due to a different electrode montage in that experiment, as compared to the study conducted by Galea et

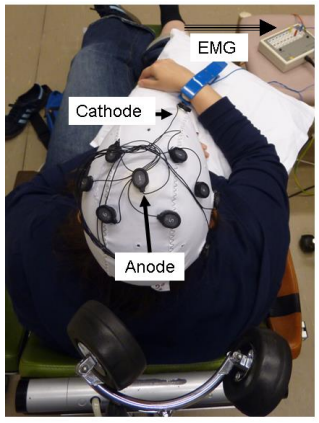

Figure 1: Experimental setup (top panel) and protocol (bottom panel)

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al [4]. In order to further investigate the effects of M1 anodal tDCS on motor performance, we conducted simultaneous electroencephalography (EEG) during self-initiated myoelectric control [5]. Our prior analysis [5] was based on resting state EEG which showed an increase of fractional power in the Theta band (4-8Hz) and decrease around "individual alpha frequency" in the Alpha band (8-13Hz) as shown by an illustrative example in Figure 2. Modeling suggests two primary effects of anodal tDCS - faster time constants of the synaptic impulse response function of the dendritic tree of the excitatory pyramidal neurons and an enhanced cortico-thalamic connectivity [5].

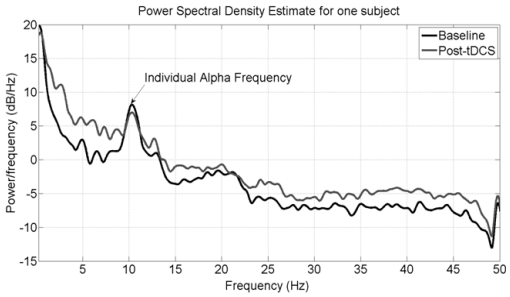

Figure 2: EEG power spectrum from experimental data of a single subject [8]

In this study, we investigated motor task-related EEG based on slow cortical potentials (SCP) [6] which are defined as those positive or negative polarizations of the EEG that last from 300ms to several seconds before EMG onset with magnitudes up to 50 μV. They originate in depolarization of the apical dendritic tree in the upper cortical layers that are caused by synchronous firing, mainly from thalamocortical afferents. SCP amplitudes are regulated within tight limits by a negative feedback-loop consisting of a cortical-basal ganglia threshold regulation system that maintains cortical activation within acceptable medium limits [7]. Functionally, they constitute a threshold regulation mechanism for local excitatory mobilization (negative slow potentials) or inhibition (positive slow potentials) of cortical networks [8].

II. Methods

A. Subjects

Ten healthy right leg-dominant male (4) and female (6) volunteers (age: 24-36 years) participated in this study after giving informed consent and all experiments were conducted in accordance with the Declaration of Helsinki. The study obtained ethics approval at the University Medical Center Goettingen, Germany. The subjects had no known neurological or psychiatric history, nor any contraindications to tDCS.

B. Experimental setup

Anodal/Sham tDCS (StarStim, Neuroelectrics, Spain) was conducted for 15min (current density=0.526A/m^2) with the anode positioned at Cz (international 10-20 system of scalp sites) and cathode over left supraorbital notch. Resting state electromyogram (EMG) was recorded at 2000Hz from the right anterior tibial muscle before, during, and immediately after anodal/sham tDCS at Cz, but prior to conduction of a self-initiated lower-extremity motor task, as shown in Figure 1. Eyes-open resting state EEG was recorded at 500Hz from the central site Cz (international 10-20) before and after anodal tDCS at Cz. During anodal tDCS at Cz, the EEG could not be recorded simultaneously from Cz but only from the nearby electrodes F3, F4, P3, P4 (international 10-20 system), which were interpolated with spherical splines [9] to estimate EEG at Cz (virtual electrode) using EEGLAB 'eeg_interp()' function [10]. For the self-initiated lower-extremity motor task, the subjects were asked to dorsiflex the ankle based on their own volition and then relax the ankle for a minimum of 5 seconds (non-verbal instruction to relax by the experimenter). A total of 50 dorsiflexions were performed by the subject in the anodal as well as sham tDCS session.

During offline analysis in Matlab R2010a (The Mathworks Inc., USA), the raw EMG sampled during each task block of the experiment was digitally zero-phase band-pass filtered (5th order Butterworth, 3 dB bandwidth = 10-500 Hz), then full-wave rectified, and then zero-phase low-pass filtered (5th order Butterworth, 3 dB frequency$_{cutoff}$ = 25 Hz) to generate its linear EMG-envelope (LE). The initiation of the dorsiflexion event was defined manually as the time instant the LE crossed above baseline LE (i.e., mean + 1 standard deviation of pre-tDCS resting-state LE). The termination of the dorsiflexion event was defined manually as the time instant the LE crossed below baseline LE. Each LE tracing was displayed on a PC monitor in random order without reference to subject or tDCS condition (sham/anodal), in order to reduce relative bias.

EEG data analysis was performed with EEGLAB and ERPLAB functions [10] to determine spontaneous fluctuations in EEG. Eye-blink artifacts were rejected using

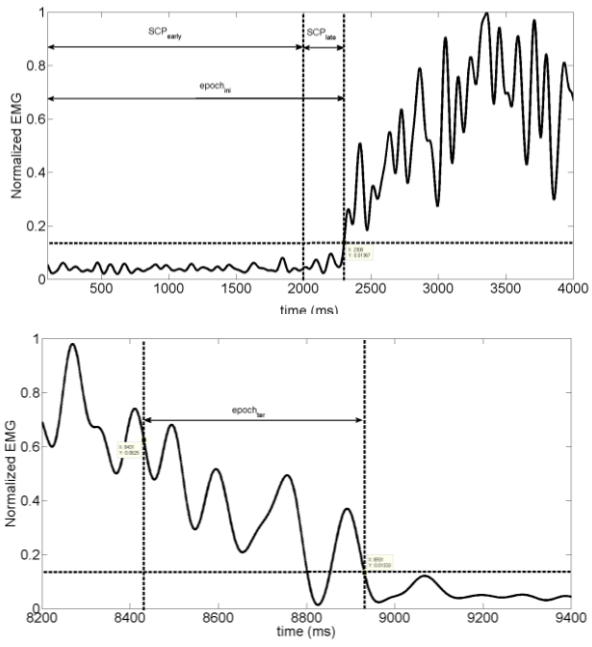

Figure 3: Linear envelope of electromyogram showing the definition of SCP$_{early}$, SCP$_{late}$, epoch$_{ini}$ and epoch$_{ter}$.

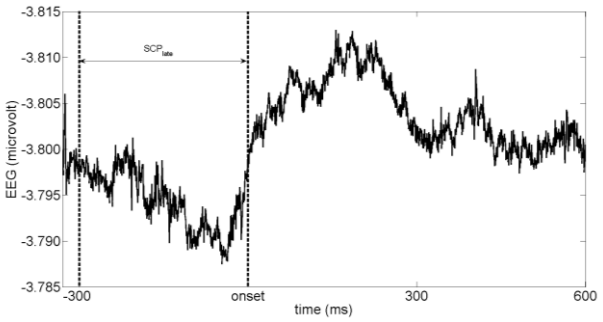

Figure 4: An illustrative single-trial late Slow Cortical Potential (SCP_{late}).

EEGLAB functions. From artifact-free resting state EEG recordings before and after anodal tDCS, the average experimental power spectrum was analyzed from 0.25Hz to 50Hz for 25 successive 4s artifact-free epochs (i.e. 100s immediately before and 100s immediately after anodal tDCS) using Welch's averaged, modified periodogram spectral estimation method (MATLAB function "spectrum.welch"). Then, the baseline-normalized change in the post-tDCS mean power in the Theta band (4-8Hz) and ±1Hz around "individual alpha frequency" in the Alpha band (8-13Hz) was computed. The artifact-free motor task-related EEG was analyzed for each trial in one 2.5 seconds epoch before initiation (i.e. $epoch_{ini}$) and another 500ms seconds epoch before termination (i.e. $epoch_{ter}$) of dorsiflexion. Here, 500ms duration for $epoch_{ter}$ was selected based on our prior work which showed that even quick termination of muscle activity can take from 492 ms to 514 ms (95% confidence interval) [2]. The first 200ms of each epoch was used for baseline correction, and then the EEG from electrodes Cz, F3, F4, P3, P4 (international 10-20 system) was averaged to compute EEG_{av}. The use of the average from several electrodes gives a more robust signal to noise ratio and reduces variability. The SCP in $epoch_{ini}$ was divided into early SCP (SCP_{early}) - from 2 seconds to 300ms before EMG onset, and late SCP (SCP_{late}) - from 300ms to 0ms before EMG onset, as defined by Jahanshahi and Hallet [11]. Then, the slope of the SCP in each epoch was estimated by fitting a first-order polynomial function to this averaged EEG (EEG_{av}) [5][6]. Based on the slope (i.e. positive or negative), each epoch was classified as either a negative or a positive epoch. The definition of SCP_{early}, SCP_{late}, and $epoch_{ter}$ are illustrated in Figure 3. The frequency of negative epochs as well as their slope in $epoch_{ini}$ and $epoch_{ter}$ were compared between anodal and sham tDCS. Two-sample t-test ('ttest2' function in Matlab) was used with the null hypothesis that anodal tDCS and sham tDCS measures are independent random samples from normal distributions with equal means and equal but unknown variances, against the alternative that the means are not equal.

III. Results

Baseline-normalized post-tDCS mean power significantly increased (60.71% vs. 8.36%; $p<0.01$) in the Theta band (4-8Hz) and decreased (-12.59% vs. -4.27%; $p<0.1$) around "individual alpha frequency" in the Alpha band (8-13Hz) when compared to sham tDCS. For motor task EEG, the slope of the negative $epoch_{ini}$ for SCP_{late} (see Figure 4) was significantly more negative (-6.43 au/sec vs. -4.86au/sec; $p=0.021$) post-tDCS when compared to sham tDCS. However, the frequency of the negative $epoch_{ini}$ for SCP_{late} was similar (close to 100%) for both anodal and sham tDCS. Moreover, anodal tDCS increased the frequency of negative $epoch_{ini}$ for SCP_{early} (76.32% vs. 62.65%; $p<0.1$) when compared to sham tDCS but did not significantly change the slope. The frequency of the negative $epoch_{ter}$ was similar (close to 0%) for both anodal and sham tDCS where anodal tDCS decreased the slope of the positive $epoch_{ter}$ (6.07au/sec vs. 8.93au/sec; $p<0.1$) when compared to sham tDCS.

IV. Discussion

In this study, we found that anodal tDCS significantly increased baseline-normalized post-tDCS mean power in the Theta band (4-8Hz) when compared to sham tDCS. Moreover, anodal tDCS increased the frequency of the negative $epoch_{ini}$ for SCP_{early}, and changed the slope of the negative $epoch_{ini}$ for SCP_{late} and of the positive $epoch_{ter}$. Principally, an apparently negative polarization of the EEG during ensemble averaging might be caused by an unequal ratio of negative and positive potential shifts [6] but we found that the frequency of the negative $epoch_{ini}$ for SCP_{late} was close to 100% and the frequency of the negative $epoch_{ter}$ was close to 0% for both anodal and sham tDCS, making this explanation unlikely. The results can be interpreted by an abstract decision-making model for self-initiated movement where an accumulator model [12] for spontaneous neural activity postulates that when the imperative to produce a movement is weak, the precise moment at which the decision threshold is crossed leading to movement is largely determined by spontaneous subthreshold fluctuations in neuronal activity. Moreover, prior work alluded to the neural correlate of evidence accumulation in the theta band where the dynamics of evidence accumulation was most strongly correlated with ramping of oscillatory power in the 4-9 Hz theta band over the course of a trial [13]. An increased baseline-normalized post-tDCS mean power in the Theta band (4-8Hz) when compared to sham tDCS may represent an urgency to respond [13], based on the Urgency-Gating Model [14]), while the oscillatory power in higher frequency bands (e.g., Beta) may reflect evidence accumulation [13].

In our prior work [5], a decrease around "individual alpha frequency" in the Alpha band (8-13Hz) was explained using a neural mass model (NMM) fitted to resting-state EEG power spectrum from all subjects. It showed that the changes from Baseline after anodal tDCS were primarily reflected by the synaptic Impulse Response Function (sIRF) of the dendritic tree of excitatory pyramidal neuron (ePN) with a decrease in its time constant (τ_{ePN}). The sIRF in the NMM approximated the low-pass response characteristics of the dendritic tree with a gain, G_i, and a time constant, τ_i, which captured the temporal spread and conduction delay of the presynaptic inputs to produce postsynaptic membrane potential alterations at the cell body. At the neuronal population level, a decrease of the time constant possibly

represented a drop in the average membrane resistance. A faster time constant of sIRF of the dendritic tree, possibly due to AMPA-mediated synapses, may lead to an enhancement of pyramidal neuron responsiveness [15]. It was therefore postulated in our prior work [5] that anodal tDCS enhanced activity, and excitability of ePN at a population level in a non-specific manner, where μ-rhythm desynchronization was suggested to be generated by the feedback loop involving the thalamo-cortical or cortico-cortical loop [16]. Moreover, an enhanced cortico-thalamic connectivity was found in our prior study [5] which could represent anodal tDCS facilitating task-specific tuning of neuronal communication under simultaneous selective attention by the subject towards the task [17]. Here, SCP originate in the depolarization of the apical dendritic tree in the upper cortical layers of ePN that are caused by synchronous firing, mainly from thalamocortical afferents [7]. Therefore, anodal tDCS may lead to changes in spontaneous subthreshold fluctuations in neuronal activity of ePN via an enhanced cortico-thalamic connectivity.

A promising avenue for model-based investigation of the spontaneous neural activity is based on accumulator model [12] which shows that a decision threshold applied to autocorrelated noise—in this case the output of a leaky stochastic accumulator—can account for the specific shape of the SCP prior to movement (called the readiness potential). Moreover, the Drift Diffusion Model (DDM) [13] posits that to make a decision, neuronal networks accumulate information until it reaches a threshold, which determines the response that corresponds to that threshold. It has been shown that DDM can explain the response times. The speed with which one accumulates evidence on average is referred to as the "drift rate" of the accumulation process. In DDM, the height of the decision threshold reflects response caution where the axonal membrane of ePN may implement a physical threshold [18]. Moreover, the DDM model, and variants of it, are capable of explaining complete response times distributions [13] where our prior work found that anodal tDCS decreased the delay in initiation of muscle contraction and increased delay in termination of muscle activity [2]. In fact, Jo and coworkers [6] alluded to the possibility that negative shifts of the SCPs are related to less effort in starting a movement as compared to positive shifts. Their results suggested that ongoing negative shifts facilitate self-initiated movement but are not related to processes underlying preparation or decision to act [6]. Here, a clear distinction in SCP correlates of decision-making processes (SCP_{early}) and movement preparation/execution (SCP_{late}) is needed vis-à-vis self-initiated versus cued tasks where information accumulation may be combined with a motor signal related to the urgency [14] to model both the task modalities. Such NIBS facilitated changes in SCP and reaction times may be promising for neurorehabilitation since SCP occurs in both executed and imagined movements, and that its magnitude and latency are related to the characteristics of the movement performed, such as speed, precision, and movement repetition [19]. Therefore, NIBS facilitated changes in SCP may be related to changes in the movement characteristics which might contribute to neurological rehabilitation by guiding brain plasticity [20].

REFERENCES

[1] M. A. Nitsche and W. Paulus, "Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation," *J. Physiol.*, vol. 527 Pt 3, pp. 633–639, Sep. 2000.

[2] A. Dutta, W. Paulus, and M. A. Nitsche, "Facilitating myoelectric-control with transcranial direct current stimulation: a preliminary study in healthy humans," *J. Neuroengineering Rehabil.*, vol. 11, no. 1, p. 13, 2014.

[3] T. Hunter, P. Sacco, M. A. Nitsche, and D. L. Turner, "Modulation of internal model formation during force field-induced motor learning by anodal transcranial direct current stimulation of primary motor cortex," *J. Physiol.*, vol. 587, no. Pt 12, pp. 2949–2961, Jun. 2009.

[4] J. M. Galea, A. Vazquez, N. Pasricha, J.-J. O. de Xivry, and P. Celnik, "Dissociating the roles of the cerebellum and motor cortex during adaptive learning: the motor cortex retains what the cerebellum learns," *Cereb. Cortex N. Y. N 1991*, vol. 21, no. 8, pp. 1761–1770, Aug. 2011.

[5] A Dutta and M. A. Nitsche, "A neural mass model for simulating modulation of cortical activity with transcranial direct current stimulation," In proceeding of: 2013 6th International IEEE/EMBS Conference on Neural Engineering (NER) 2013.

[6] H.-G. Jo, T. Hinterberger, M. Wittmann, T. L. Borghardt, and S. Schmidt, "Spontaneous EEG fluctuations determine the readiness potential: is preconscious brain activation a preparation process to move?," *Exp. Brain Res.*, vol. 231, no. 4, pp. 495–500, Dec. 2013.

[7] N. Birbaumer, T. Elbert, A. G. Canavan, and B. Rockstroh, "Slow potentials of the cerebral cortex and behavior," *Physiol. Rev.*, vol. 70, no. 1, pp. 1–41, Jan. 1990.

[8] N. Birbaumer, "slow Cortical Potentials: Plasticity, Operant Control, and Behavioral Effects," *The Neuroscientist*, vol. 5, no. 2, pp. 74–78, Mar. 1999.

[9] M. Scherg, N. Ille, H. Bornfleth, and P. Berg, "Advanced tools for digital EEG review: virtual source montages, whole-head mapping, correlation, and phase analysis," *J. Clin. Neurophysiol. Off. Publ. Am. Electroencephalogr. Soc.*, vol. 19, no. 2, pp. 91–112, Apr. 2002.

[10] A. Delorme and S. Makeig, "EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," *J. Neurosci. Methods*, vol. 134, no. 1, pp. 9–21, Mar. 2004.

[11] M. Jahanshahi and M. Hallett, *The Bereitschaftspotential: Movement-Related Cortical Potentials*. Springer, 2003.

[12] A. Schurger, J. D. Sitt, and S. Dehaene, "An accumulator model for spontaneous neural activity prior to self-initiated movement," *Proc. Natl. Acad. Sci. U. S. A.*, vol. 109, no. 42, pp. E2904–2913, Oct. 2012.

[13] M. K. van Vugt, P. Simen, L. E. Nystrom, P. Holmes, and J. D. Cohen, "EEG oscillations reveal neural correlates of evidence accumulation," *Front. Neurosci.*, vol. 6, p. 106, 2012.

[14] P. Cisek, G. A. Puskas, and S. El-Murr, "Decisions in Changing Conditions: The Urgency-Gating Model," *J. Neurosci.*, vol. 29, no. 37, pp. 11560–11571, Sep. 2009.

[15] N. Hô and A. Destexhe, "Synaptic background activity enhances the responsiveness of neocortical pyramidal neurons," *J. Neurophysiol.*, vol. 84, no. 3, pp. 1488–1496, Sep. 2000.

[16] J. Matsumoto, T. Fujiwara, O. Takahashi, M. Liu, A. Kimura, and J. Ushiba, "Modulation of mu rhythm desynchronization during motor imagery by transcranial direct current stimulation," *J. Neuroengineering Rehabil.*, vol. 7, p. 27, 2010.

[17] F. Briggs, G. R. Mangun, and W. M. Usrey, "Attention enhances synaptic efficacy and the signal-to-noise ratio in neural circuits," *Nature*, vol. 499, no. 7459, pp. 476–480, Jul. 2013.

[18] P. Simen, "Evidence Accumulator or Decision Threshold - Which Cortical Mechanism are We Observing?," *Front. Psychol.*, vol. 3, p. 183, 2012.

[19] Y. Gu, D. Farina, A. R. Murguialday, K. Dremstrup, and N. Birbaumer, "Comparison of movement related cortical potential in healthy people and amyotrophic lateral sclerosis patients," *Front. Neurosci.*, vol. 7, p. 65, 2013.

[20] J. J. Daly and J. R. Wolpaw, "Brain-computer interfaces in neurological rehabilitation," *Lancet Neurol.*, vol. 7, no. 11, pp. 1032–1043, Nov. 2008.