Local and Remote Effects of Transcranial Direct Current Stimulation on the Electrical Activity of the Motor Cortical Network

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Abstract: We systematically investigated the effects of cathodal and anodal Transcranial Direct Current Stimulation (CtDCS, AtDCS) on the electric activity of primary motor cortex during a motor task. High-density electroencephalography was used to define the spatial diffusion of tDCS after effects. Ten healthy subjects performed a finger tapping task with the right hand before and after three separate sessions of 20 minutes of Sham, AtDCS or CtDCS over left primary motor cortex (M1). During movement, we found an increment of low alpha band Event-Related Desynchronization (ERD) in bilateral central, frontal areas and in the left inferior parietal region, as well as an increment of beta ERD in fronto-central and parieto-occipital regions, after AtDCS compared to Sham and CtDCS. In the rest pre-movement period, after Sham as well as AtDCS, we documented an increment of low alpha band power over the course of pre- and post-stimulation recording sessions, localized in the sensorimotor and parieto-occipital regions. On the contrary, after CtDCS no increment of low alpha power was found. Finally beta band coherence among signals from left sensorimotor cortex and activity of bilateral parietal, occipital and right frontal regions was higher after AtDCS compared with Sham condition. Similarly, theta coherence with parietal and frontal regions was enhanced after AtDCS. We hypothesize that the local modulation of membrane polarization, as well as long-lasting synaptic modification induced by tDCS over M1, could result in changes of both local band power and functional architecture of the motor network. *Hum Brain Mapp* 35:2220–2232, 2014. © 2013 Wiley Periodicals, Inc.

Key words: tDCS; high-density EEG; functional connectivity; Event Related Desynchronization/Synchronization; imaginary part of coherence

INTRODUCTION

Transcranial Direct Current Stimulation (tDCS) modifies the membrane excitability of neuronal cells by a prolonged,

low intensity, electric current (1–2 mA) delivered through a pair of electrodes placed on the scalp (Paulus, 2003). The direction of changes in excitability is determined by the polarity of the current. Anodal tDCS (AtDCS) results in a membrane depolarization (excitation), whereas Cathodal tDCS (CtDCS) induces hyperpolarization (inhibition), of the cortical neurons near the anode or cathode electrode (Nitsche et al., 2001, 2003; Nitsche & Paulus, 2000). Long lasting after-effects of tDCS, likely mediated by changes at the synaptic level, have been described: AtDCS leads to a reduction of intracortical inhibition and to an increment of intracortical facilitation, whereas CtDCS has the opposite effects (Di Lazzaro et al., 2012a; Liebetanz et al., 2002). The stability and duration of tDCS changes in cortical

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excitability depend on the duration of the stimulation and the intensity of the applied current (Bindman et al., 1964). The after-effects of tDCS are thought to be mediated by N-methyl-D-aspartate (NMDA) glutamate receptors, but the mechanisms underlying these changes are poorly known (Liebetanz et al., 2002; Nitsche et al., 2003; Siebner et al., 2004).

Local polarity-dependent changes of cortical excitability after the stimulation of primary motor (M1) cortex have been already documented (Di Lazzaro et al., 2012b): AtDCS induces an increment of the amplitude of motor evoked potentials whereas CtDCS has the opposite effect (Nitsche & Paulus, 2000; Quartarone et al., 2004). The AtDCS effects at cortical level are associated with an improvement of motor performance, isometric force endurance, motor learning and consolidation (Boggio et al., 2006; Cogiamanian et al., 2007; Reis et al., 2009; Reis & Fritsch, 2011; Stagg et al., 2011; Tecchio et al., 2010). It can be hypothesized that these changes are related to a more diffuse modulation of neuronal activity. Excitability changes of local neural activity could also induce changes in areas distant from – but functionally related to – the stimulated area, giving rise to a transient reconfiguration of the brain motor network. In support of this hypothesis are the widespread increases or decreases of regional Cerebral Blood Flow in cortical and subcortical areas, documented respectively after AtDCS or CtDCS of M1 (Lang et al., 2005). Similarly a blood oxygenation level dependent (BOLD) signal increase/decrease has been described after anodal/cathodal tDCS not only in the stimulated motor region, but also in nearby functionally related areas (Baudewig et al., 2001). AtDCS on the prefrontal dorsolateral cortex causes an increased synchrony within the brain areas engaged in focused attention, as revealed by functional Magnetic Resonance Imaging (fMRI), as well as a reduced synchrony in the default-mode network, which is deactivated during task periods and related to cognitive functions (Keeser et al., 2011; Peña-Gómez et al., 2012). Moreover, as estimated from fMRI data by graph theoretical analysis (Polanía et al., 2012), AtDCS on M1 boosts long distance functional connections; while EEG revealed an increase of the connectivity of electrical activity in the 60–90 Hz range among premotor, motor and sensorimotor cortices (Polanía et al., 2011, 2012).

The present study aims at systematically investigating the effects of cathodal and anodal tDCS on the electric activity of the whole motor cortical network during a motor task, thus assessing possible long-range tDCS effects. We used high-density EEG to map changes of cortical rhythmic activity on the entire brain. Indeed, cortical rhythms are the product of synchronized electric activity among and within neuronal assemblies, and their power modulation is assumed to reflect the underlying changes in neuronal synchrony, as revealed by Event-Related Desynchronization (ERD) or Event-Related Synchronization (ERS) (Neuper & Pfurtscheller, 2001). In particular, the ERD phenomenon in alpha (8–13 Hz) and beta (13–30 Hz) bands for the sensorimotor cortices in preparation of and during a movement, as well as during movement imagination or observation, has been extensively described (Pfurtscheller & Aranibar, 1979;

Pfurtscheller & Berghold, 1989; Toro et al., 1994). Similarly, ERS in alpha or beta bands after voluntary movement and after somatosensory stimulation has been observed in the same areas and has been interpreted as a state of inhibition of neural circuitry in the sensorimotor cortex (Leocani et al., 1997; Pfurtscheller et al., 1996; Pfurtscheller & Lopes da Silva, 1999). However, the after-effects of tDCS on the modulation of local oscillatory electric activity of motor cortices during movement have been little investigated. Evidence for an increment of rolandic ERD after AtDCS and a decrement after CtDCS have been only documented during movement imagination (Matsumoto et al., 2010).

In this study we also focused on the effect of tDCS on the connectivity between M1 and all other cerebral sites. Functional connectivity is defined as the temporal correlation between the activity of distinct neural assemblies, in terms of statistically significant dependency between distant brain areas. If different cortical regions display correlated band limited oscillatory activities, we can argue that they participate to the same functional network. We hypothesize that the local modulation of membrane polarization, as well as long-lasting synaptic modification induced by tDCS over M1, could result in changes not only of local band power, but also of M1 connectivity with related functionally connected areas.

MATERIALS AND METHODS

Experimental Procedure

Ten healthy subjects (mean age 29.7 ± 3.4 years, male males) participated to the study after giving written informed consent. All subjects were right-handed (Edinburgh Manuality Test, Oldfield, 1971 : 92.5 median, [68–100] 5–95% percentile), did not have history of neurological disorder or head injury and were not taking any CNS affecting drug. Each subject participated in three sessions (Cathodal, Anodal, or Sham stimulation) randomly presented. The time occurring between two consecutive sessions was >2 weeks. In each session, high-density EEG was recorded during a finger tapping task performed by the right hand before and after tDCS. Specifically, the stimulation was carried out soon after the EEG recording. To avoid electrode polarization due to the direct current, the EEG net was removed before and applied again after the stimulation. The time between the end of the tDCS and the starting of EEG recording was of about half an hour.

During the EEG recording, lasting 12 minutes, a tone beep drove the subject to intermingle periods of 12 seconds of rest to periods of 12 seconds of movement. The movement was a rhythmic thumb opposition toward the other fingers in a predefined sequence (index, middle finger, ring, little finger, ring, middle finger, index). Subject was required to maintain a self-paced frequency of about 2 Hz and to watch his/her hand during movement. A video synchronized to EEG recorded the hand to check for correct sequence execution.

Direct current of 1 mA intensity was delivered for 20 minutes by a battery driven stimulator (Eldith DC Stimulator, Neuro Conn, Germany) through saline soaked sponge electrodes of surface $7 \times 5 \text{ cm}^2$. The active electrode was located over the left primary motor cortex (C3 scalp position of the International 10/20 EEG system) with the 7 cm long side placed along the central sulcus. The reference electrode was positioned over the right supraorbital region. Sham stimulation was realized by delivering the current for 15 seconds both at the begin and the end of the 20 minutes of stimulation to induce the short-lasting tingling perceived during the transient period of current turn-on and off in the real stimulation. At the end of each session, it was asked to the subject whether in his/her opinion he/she had received a real or sham stimulation.

EEG recordings were performed by means of a 128 electrode net (Electrical Geodesics, version 1.1). The position of each electrode and of four anatomical landmarks (preauricular points, nasion, vertex) were digitized by means of a 3D digitizer (Polhemus, 3Space Fastrak).

Skin/electrode impedance was measured before each EEG recording and kept below 100 k Ω . EEG data were sampled at 500 Hz and processed off-line.

Data Analysis

A semiautomatic Independent Component Analysis-based procedure (Barbati et al., 2004) was applied to identify and to remove cardiac and/or ocular artifacts, as well as activity coming from contraction of head muscles during movement. Saturated or corrupted EEG epochs were rejected by visual inspection. EEG signals were transformed to the common average reference.

Band limited power analysis

The signal recorded from each sensor was segmented into intervals locked to the movement onset and offset, from 3 seconds before to 9 seconds after the movement onset, and from 2 seconds before to 8 seconds after the movement offset. The time–frequency representation (TFR) was calculated in the above defined time intervals and in the frequency range from 1 to 45 Hz by using a complex wavelet analysis (Tallon-Baudry et al., 1997). The power of TFR was obtained as the squared magnitude of the complex wavelet-transformed data and normalized by the mean power in the period from –2.5 to 0 s before the movement onset. The aim of TFR analysis was to find time intervals during and after movement, in which sustained and stable ERD/ERS were present. Thus, the following three time intervals were chosen: the rest period, from 2.5 to 0.5 s before movement onset (*Rest*); the movement period, from 2 to 4 s after the movement onset (*Mov*); the post-movement period, from 2 to 4 s after the end of the movement (*MovOff*). The “rest” period we choose is not a true “resting state” period (Wang et al., 2012), because of the high level of expectation and arousal. However, in this

period of time, we can assume that any activation related to the task or the preparation of movement is absent.

In the three time intervals, the Power Spectral Densities (PSDs) of each EEG channel were estimated from raw signals by applying the Welch method (Hanning window, 50% overlap, 1 Hz frequency resolution). Afterward, the band powers (*P*) were obtained for each time interval and each EEG electrode by averaging the PSD values across frequency bands. For each subject, the individual alpha peak was estimated (Individual Alpha Frequency, IAF, Klimesch, 1999). Accordingly, the frequency bands were defined as follows: delta (2–4.5 Hz), theta (5 to 7.5 Hz), low alpha (IAF–2 to IAF), high alpha (IAF to IAF+2), beta (15–25 Hz), and gamma (31–45 Hz). The IAF variability over the group of subjects, measured as mean value $\pm$ standard deviation, was 10.35 ± 0.68 Hz. Thus, ERD and ERS values in each band were obtained according to Pfurtscheller and Lopes da Silva (1999):

$$\text{ERD} = 100 \frac{(P_{\text{Mov}} - P_{\text{Rest}})}{P_{\text{Rest}}}$$

$$\text{ERS} = 100 \frac{(P_{\text{MovOff}} - P_{\text{Rest}})}{P_{\text{Rest}}}$$

Band power and ERD/ERS values were calculated for each EEG session (before and after Sham, CtDCS and AtDCS).

Functional connectivity

Functional connectivity between left motor cortex and the whole brain was obtained by estimating coherence (i.e. correlation in frequency domain) between the signal from the C3 electrode and the signals of all the other EEG channels in the three above defined time intervals.

Given the two time domain signals, $x_{C3}(t)$ and $x_j(t)$ (*j* denoting each EEG channel) and their Fourier transforms, $X_{C3}(f)$ and $X_j(f)$, coherence is a complex valued measure of interaction defined as

$$C_{C3j}(f) \equiv \frac{S_{C3j}(f)}{\sqrt{S_{C3C3}(f) S_{jj}(f)}}$$

where

$$S_{C3j}(f) \equiv \langle X_{C3}(f) X_j^*(f) \rangle$$

is the cross spectrum between $X_{C3}(f)$ and $X_j(f)$, $S_{C3C3}(f)$ is the power spectrum of $X_{C3}(f)$ and $S_{jj}(f)$ is the power spectrum of $X_j(f)$. The symbols $*$ and $\langle \rangle$ indicate complex conjugation and expectation value, respectively. In practice, expectation value was estimated as the average over 1 second long trials (linear detrending, Hanning windowing, 50% overlapping) in the considered time intervals.

A non-vanishing imaginary component (*ImCoh*) of complex coherence $C_{C3j}(f)$ can only indicate a phase-shifted

relation between X_{C3} and X_j . As a consequence of this property, ImCoh is a measure of functional connectivity robust to self-connectivity induced by volume conduction (Guggisberg et al., 2008; Martino et al., 2011; Marzetti et al., 2007, 2008; Nolte et al., 2004).

Here, we used a corrected version of the imaginary part of coherence (Ewald et al., 2012; Pascual-Marqui, 2007) given, for each frequency, by:

$$\text{cImCoh}_{C3j} \equiv \frac{C_{C3j}^I}{\sqrt{(1 - C_{C3j}^R)}}$$

where the superscripts R and I indicate real and imaginary part, respectively. The functional connectivity measure was obtained by averaging the absolute value of cImCoh across frequencies within each frequency band.

To evaluate whether the stimulation affects coherence modulation during and after the movement, the event related cImCoh (ER- cImCoh) was evaluated by the difference of cImCoh values during and after movement, $\text{cImCoh}_{\text{Mov}}$ and $\text{cImCoh}_{\text{MovOff}}$, respectively, with respect to cImCoh in the rest period, $\text{cImCoh}_{\text{Rest}}$ (Nolte et al., 2004; Pfurtscheller & Andrew, 1999). We thus obtained cImCoh and event related cImCoh (ER- cImCoh) values for each EEG session, before and after each type of stimulation: AtDCS, CtDCS, Sham.

Source analysis

To localize the sources of brain rhythmic activity we performed a current density analysis in 3D MNI space using sLORETA (Pascual-Marqui, 2002). The current source density distribution of each frequency band power in the above defined time intervals was estimated on a grid of 6239 voxels, with a spatial resolution of 5 mm. Post versus pre-stimulation difference of ERD/ERS and band power values at rest were then evaluated for each voxel. Cortical maps of differences between conditions (CtDCS vs Sham or AtDCS vs Sham) were finally calculated.

Statistical analysis

Values of power in the pre-movement period (P_{rest}), log-transformed in order to fit a Gaussian distribution, and coherence were compared across conditions to test the effect of the different stimulations (CtDCS, Sham or AtDCS) on band power and connectivity. Similarly, values of ERD/ERS and event related cImCoh were compared across conditions to test the effect of the different stimulation on both band power and coherence modulation during and after movement. For this purpose, for each stimulation session (CtDCS, Sham, and AtDCS) a cluster-based nonparametric randomization test taking into account the multiple-comparisons problem was used (Maris and Oostenveld, 2007). The test, available in FieldTrip (<http://www.ru.nl/neuroimaging/fieldtrip>, Oostenveld et al., 2011) – an open-source Matlab

toolbox developed at the Donders Institute for Brain, Cognition, and Behaviour (Nijmegen, The Netherlands) – was applied to establish the topography of sensors in which the considered parameters (P_{Rest} , ERD, ERS, ER- cImCoh , $\text{cImCoh}_{\text{Rest}}$ in each band) showed a significant difference between pre- and post-stimulation. For each sensor the post- versus pre-stimulation condition was tested by a dependent-sample t -value. All samples showing a t -value greater than a threshold corresponding to $P = 0.05$ (uncorrected) were selected and spatially clustered. The level of the statistics of the cluster was defined as the sum of t -values within the cluster. The cluster with the maximum value was used to construct the statistics. A reference distribution of maximum cluster t -values was obtained by randomization of data across the two condition for 500 times and was used to evaluate the statistic of the actual data. The non-parametric test was also applied to evaluate the topography of post- versus pre-stimulation differences between the real and sham stimulation (CtDCS vs Sham or AtDCS vs Sham).

The values of all the calculated parameters were averaged over EEG sensors grouped on the basis of regions of interest (ROIs) defining different macro-areas: left and right fronto-polar cortex (three electrodes closest to Fp1 and Fp2 position), left, right and medial fronto-central cortex (four electrodes closest to FC3-F3, FC4-F4 and FCz-Fz positions), left and right central regions, corresponding to sensorimotor cortices (two electrodes closest to C3 and C4 positions), left, right and medial superior parietal cortex (seven electrodes closest to P3-P1 and P4-P2 positions) and four electrodes closest to Pz-POz position), left and right inferior parietal cortex (two electrodes closest to P7 and P8 position), occipital areas (five electrodes closest to O1, O2 positions). The differences of these averaged values between post stimulation and pre-stimulation were then calculated. Finally, ROIs with electrodes displaying significant difference in the non-parametric test were entered in an ANOVA design for repeated measures. ROIs and Stimulation Type (AtDCS, CtDCS, Sham) were the within-subject factors.

RESULTS

All subjects well tolerated the stimulation, not reporting any discomfort during the experiment. Nobody was able to distinguish whether he/she had received real or sham stimulation.

Event-Related Desynchronization/Synchronization and Event-Related cImCoh

ERD/ERS and ER- cImCoh before tDCS

No difference in patterns of power modulation or event related coherence before stimulation was observed, in comparing the different sessions. Specifically, TFR

Figure 1.

revealed a sustained alpha (8–13 Hz) and beta (15–25 Hz) band power suppression during the whole movement period with respect to the pre-movement baseline (alpha and beta ERD) and an enhanced beta activity after the end of movement from about 1.5 to 4 s (beta ERS, Fig. 1A). This temporal structure of ERD/ERS for sustained movement was also observed by Erbil and Ungan (2007). Topographically, low alpha ERD was observed in bilateral centro-parietal and parieto-occipital regions, high alpha ERD in bilateral central regions, beta ERD in bilateral centro-frontal regions and beta ERS in the sensorimotor region contralateral to the movement (Fig. 1B,C). Moreover, specific patterns of ER-clmCoh were found: (1) an increased ER-clmCoh in low alpha band between left motor area and right somatosensory and left frontal regions; (2) a reduced ER-clmCoh in low alpha band between left motor area and parieto-occipital region; (3) an enhanced ER-clmCoh in high alpha and beta band between left motor area and contralateral hemisphere; (4) an enhanced ER-clmCoh in beta band between left motor area and left central regions after the end of the movement (Fig. 1B).

ERD/ERS and ER-clmCoh after tDCS

The non parametric randomization test revealed a specific topography of low alpha ERD changes due to stimulation. In particular, an increased low alpha ERD with respect to the pre-stimulation was observed in bilateral parieto-frontal regions after AtDCs, whilst no differences were observed after Sham and CtDCS (Fig. 2A, Left, first row). The post- *versus* pre-stimulation low alpha ERD difference was greater for AtDCS than for Sham in bilateral medial centro-frontal regions and left inferior parietal region (Fig. 2A, Left, second row).

ANOVA on post *vs* pre stimulation low alpha ERD differences showed a *Stimulation type* effect [$F(2,18) = 4.234$; $P = 0.031$], being AtDCS condition different from both Sham and CtDCS (Post-hoc comparisons, $P = 0.035$, and $P = 0.008$ respectively, Fig. 2A Right).

Source localization showed that the increased ERD in low alpha band after AtDCS was localized in the left sensorimotor (post-central and pre-central gyrus), bilateral medial premotor and supplementary motor areas, as well as in the left inferior parietal lobule (Fig. 2C, Left).

Similarly, an increased beta ERD was observed in fronto-central and parieto-occipital regions after AtDCs

(Fig. 2B). Source localization showed that the increased ERD in beta band after AtDCS was localized in the medial premotor and supplementary motor areas, as well as left inferior parietal cortex (Fig. 2C, Right). ANOVA on post *vs* pre stimulation beta ERD differences showed a *Stimulation type* effect [$F(2,18) = 3.800$; $P = 0.042$], being AtDCS condition different from both Sham and CtDCS (Post-hoc comparisons, $P = 0.046$, and $P = 0.048$, respectively, Fig. 2B Right).

No differences were found in beta ERS as well as in ER-clmCoh during and after movement, in comparing post with pre stimulation conditions, for Sham, AtDCS or CtDCS.

Band Power and clmCoh in the Baseline Period at Rest

At rest (in the pre-movement period), a significant increment of low alpha power was found after Sham and AtDCS in segregated topographical clusters, as revealed by the non-parametric randomization test (Fig. 3A, Left, first row). In particular, for these two conditions (Sham and AtDCS) low alpha band power was significantly higher in post than in pre stimulation over left sensorimotor, premotor and supplementary motor regions and in medial and parietal areas (Pz, POz, P2,P4 electrodes). No differences were found for CtDCs.

By comparing the post versus pre stimulation low alpha power difference among the conditions, we observed a low alpha reduction in CtDCS condition with respect to Sham (Fig. 3A Left, second row). No differences were observed between AtDCS and Sham.

ANOVA on post versus pre differences low alpha power confirmed the *Stimulation type* effect [$F(2,18) = 5.706$; $P = 0.012$], being CtDCS condition different from Sham and AtDCS (post-hoc comparison $P = 0.033$, and $P = 0.020$, respectively, Fig. 3, Right). Source localization showed that alpha power decrease was localized in the left primary sensorimotor regions and central-parietal regions corresponding to precuneus (Fig. 3B). No difference between pre-and post-stimulation power depending on stimulation type was observed in the other frequency bands.

After AtDCS, a clmCoh increase in beta band with respect to Sham condition was observed between left motor and both the parietal areas and right frontal areas

Figure 1.

(A) Grand average over subjects and across the pre-stimulation conditions of all the type of stimulations (Cathodal, Sham, and Anodal) of TFR of power modulation for EEG signal corresponding to C3 position. The time intervals shown in the figure range from 2.5 s before to 9 s after the movement onset and from 2 s before to 8 s after the movement offset. (B) Topographies of low alpha ERD, high alpha ERD, beta ERD, beta ERS,

event related clmCoh in the time windows marked by the box in the TFR during movement (ERD) and after the movement offset (ERS). In clmCoh plots the black full circle indicates the C3 electrode position. (C) Brain sources of low and high alpha and beta ERD during movement and beta ERS after movement, as revealed by sLORETA.

(Fig. 4 Left). ANOVA design confirmed the *Stimulation type* effect [$F(2,18) = 8.898$; $P = 0.002$], being AtDCS different both from Sham and CtDCS (post-hoc comparisons $P = 0.002$ and $P = 0.011$, respectively, Fig. 4, Right).

Similar patterns of coherence modulation were observed in theta band, where a higher increased cImCoh between left motor area and both bilateral frontal and medial parietal areas were found after AtDCS with respect to Sham (Fig. 4, Left). In particular, ANOVA showed the *Stimulation type* effect [$F(2,18) = 6.830$; $P = 0.006$], being AtDCS different from Sham ($P = 0.007$, Fig. 4, Right).

DISCUSSION

This study aimed at investigating the after-effects of tDCS, applied over the left primary motor cortex, on the neuronal electric activity of the stimulated site during a motor task. We focused on ERD changes during movement and showed an increment of ERD in low alpha and beta bands after AtDCS but not after CtDCS or Sham. This effect was found in sensorimotor related regions, i.e. inferior parietal, pre-central areas (motor, premotor, and supplementary motor cortices), as well as in parieto-occipital areas for beta band. It has been suggested that alpha and beta ERD during the execution of a movement are correlated with the activation of the cortical areas recruited for the task (Pfurtscheller, 1992; Pfurtscheller et al., 1996). The ERD is related to changes of one or more parameters controlling the oscillations in neural networks (Lopes da Silva, 1991): the intrinsic properties of the membranes of neurons; the magnitude of synaptic connections between neurons (cortico-cortical and thalamo-cortical); the action of modulating local and systemic neurotransmitters (Pfurtscheller & Lopes da Silva, 1999). We hypothesize that the observed after-effects of AtDCS on low alpha and beta ERD are due to intracortical facilitation mediated by NMDA receptors (Liebetanz et al., 2002). This might result in an improvement of synaptic efficiency, paired to a more widespread ERD during the task, explaining the improvement in motor performance previously described after AtDCS on the motor cortex (Reis & Fritsch, 2011). According to the diffuse nature of low alpha rhythm, the widespread increase of ERD after AtDCS was found only in low and not in high alpha band. Indeed as evidenced by several studies, the modulation of alpha rhythm is not an unitary phenomenon (Hummel et al., 2002; Klimesch et al., 1998; Neuper & Pfurtscheller, 2001; Pineda, 2005). Low alpha rhythm ERD during a visuo-motor task is more widespread than high alpha ERD, which is clearly confined over the motor areas supporting the specific movement (Babiloni et al., 1999; Pfurtscheller et al., 1999). The low alpha desynchronization found over sensorimotor, frontal and parietal areas probably reflects general demands for task execution and attention processes (Neuper & Pfurtscheller, 2001; Pfurtscheller et al., 1999). We did not find any effect of stimulation on beta ERS. It has

been suggested that beta ERS may be an indicator for the level of motor cortex excitability. Indeed, Hari et al. (1998) found that beta rebound after median nerve stimulation was suppressed during finger movement. Since tDCS affects motor cortex excitability, an effect also on beta ERS may be expected. However, the motor task used in this study implies a prolonged activation of the motor cortex, as the stable alpha and beta ERD demonstrate. The somatosensory inputs and somato-motor integration play an essential role in generating post-movement beta ERS (Cassim et al., 2000) and in our motor task the prolonged proprioceptive input could affect the intensity of beta rebound and would mask a possible effect of stimulation.

We also documented stimulus dependent changes of alpha band power at rest. Specifically, in sham condition an alpha power increment in the rest period across time was found in the motor, premotor and parietal regions. Alpha power has been traditionally interpreted as a functional correlate of “relaxed wakefulness” (Lindsley, 1960). According to this view, the observed increment of alpha power after AtDCS or Sham over sensorimotor and parietal areas could be related to a progressive wandering of attention and decline in arousal, resulting in a disengagement of these cortical areas. Recent studies showed that alpha power modulation is a functionally relevant sensory gating mechanism deployed by attention in somatosensory areas and could be related to mechanisms reflecting the advancing of task-related neurocognitive strategies (Haegeens et al., 2011; Jones et al., 2010; van Ede et al., 2011). An enhancement of alpha activity over sensorimotor areas has also been documented over time during practicing of visuomotor tasks (Slobounov et al., 2007; Smith et al., 1999). Wan et al. (2011) documented an increment of alpha power in somatosensory regions across a single, 1 hour lasting recording session during an attention somatosensory task. These studies suggested that a steady increment in alpha power over sensorimotor cortices would reflect active inhibition of specific cortical regions due to a progressive efficiency of brain dynamics over time. Similarly, for parietal regions alpha activity has been linked to efficient executive control, since increasing alpha facilitates goal-directed behavior (Dockree et al., 2007). Sadaghiani et al. (2010) documented a link between parieto-occipital alpha oscillation and a network at rest comprising dorsal anterior cingulate cortex, anterior insula, anterior prefrontal cortex and thalamus, and suggested that tonic alertness is related to alpha oscillations, which reduce distraction and enhance detection of relevant sensory stimuli by synchronously clearing the flood of information. On the light of the above mentioned evidence, we can argue that the low alpha power increase is a functional process of efficiency, not altered by anodal stimulation. On the contrary, since after CtDCS we did not observe any increment of low alpha power across time in comparison with sham and AtDCS conditions, we can hypothesize that CtDCS disrupts this process and reduces its efficiency in the allocation of resources for the accomplishment of the task.

Figure 2.

(A) Left: First row: *T*-values topographies from comparison of post versus pre-stimulation low alpha ERD for cathodal, sham and anodal stimulation. Second row: *T*-values topographies from post versus pre stimulation alpha ERD differences by respectively comparing CtDCS with Sham and AtDCS with Sham. Sensors showing significant difference between conditions in the non-parametric test after randomization are marked by a cross. Right: Mean (standard error) post vs pre low alpha ERD differences in Sham (white boxes), cathodal (black boxes) and anodal (gray boxes) stimulation for fronto-central and parietal areas. Stars and crosses indicate significant difference between conditions ($*P < 0.05$, $+P < 0.10$) in the paired *t*-test. **(B)** First row: *T*-values topographies from comparison of post versus pre-stimulation beta ERD for cathodal, sham and anodal stimulation.

Second row: *T*-values topographies from post versus pre stimulation alpha ERD differences by respectively comparing CtDCS with Sham and AtDCS with Sham. Sensors showing significant difference between conditions in the non-parametric test after randomization are marked by a cross. Right: Mean (standard error) post vs pre beta ERD differences in Sham (white boxes), CtDCS (black boxes) and AtDCS (gray boxes) stimulation for fronto-central, parietal and occipital areas. Stars and crosses indicate significant difference between conditions ($*P < 0.05$, $+P < 0.10$) in the paired *t*-test. **(C)** Brain sources of low alpha ERD (left) and beta ERD (right) modulation after AtDCS with respect to Sham, obtained by comparing the post vs pre low alpha ERD differences at the voxel level. Values of band power at the voxel level were obtained by sLORETA.

Figure 3.

(A) Left: First row: *T*-values topographies from comparison of post versus pre-stimulation low alpha band power at rest for CtDCS, Sham and AtDCS. Second row: *T*-values topographies from post versus pre stimulation low alpha power differences by respectively comparing CtDCS with Sham and AtDCS with Sham. Sensors showing significant difference between conditions in the non-parametric test after randomization are marked by a cross. Right: Mean (standard error) post versus pre low alpha

band percentage difference in Sham (white boxes), CtDCS (black boxes) and AtDCS (gray boxes) stimulation for left central areas and medial parietal areas. Stars and crosses indicate significant difference between conditions ($*P < 0.05$, $+P < 0.10$) in the paired *t*-test. **(B)** Brain sources of low alpha reduction after CtDCS compared with Sham, obtained by comparing the post versus pre differences of low alpha brain source activity, estimated by sLORETA.

Finally, we observed this effect of alpha disruption also in the precuneus, the activity of which is likely to reflect an intrinsic state associated with alertness and self-related processes (Gusnard et al., 2001; Raichle et al., 2001).

We found at rest a significant increase of coherence in beta and theta bands only after AtDCS. We hypothesized that AtDCS might strengthen the synaptic connections of functionally linked cortical areas, probably inducing a change in functional architecture of the whole motor network and its communication with other networks. Specifically, a significant increase after AtDCS in beta band

coherence was documented between the activity recorded over the stimulated left primary motor cortex and sensori-motor cortices, parietal and prefrontal cortical areas. Indeed, transcranial magnetic stimulation studies (Koch et al. 2009a; Koch & Rothwell, 2009b) documented functional connections between parietal cortex and its sub-regions, such as posterior parietal cortex and different portions of the intra-parietal sulcus, and the ipsilateral, or even the contralateral primary motor cortex. TDCS of right parietal cortex induces changes of M1 excitability during motor imagery and action observation (Feurra et al., 2011).

Figure 4.

Left: T-values topographies from differences between post and pre stimulation beta and theta coherence at rest by comparing AtDCS with Sham. Sensors showing significant difference between conditions in the non-parametric test after randomization are marked by a cross. Black full circle indicates the C3 electrode position. Right: Mean (standard error) post versus pre

stimulation beta and theta coherence at rest in Sham (white boxes), CtDCS (black boxes) and AtDCS (gray boxes) stimulation for frontal, parietal and occipital areas. Stars and crosses indicate significant difference between conditions (* $P < 0.05$, + $P < 0.10$) in the paired t-test.

Previous task related studies demonstrated a beta band specific functional connection among frontal and somato-sensory areas, corresponding to the same cortical areas in which we found an increased coherence (Babiloni et al., 2005). Even though the functional role of oscillations in beta band is yet elusive (Brovelli et al., 2004; Engel & Fries, 2010), beta activity has been traditionally associated to motor processing (Baker, 2007; Pfurtscheller et al., 1996), sensorimotor control (Chakarov et al., 2009) and cortico-spinal coupling (Schoffelen et al., 2005). Moreover, the enhanced theta band connectivity between left motor and both parietal and frontal regions after AtDCS could account for a role of slower frequency coherent oscillations in mediating the neural representations of hand kinematics (Jerbi et al., 2007). Further analysis and ad hoc designed studies are needed to address this point.

Finally, the montage of the stimulating electrodes (anode over left primary motor cortex, cathode over right supra-orbital region) might also suggest an electric path going through midline structures in the frontal lobe, including supplementary motor area (SMA) and anterior cingulate cortex. The short and long range modulation of oscillatory activity we found could be also partially mediated by the direct stimulation of these areas, which play an important role in planning, initiation, and execution of motor acts. Indeed, SMA and anterior cingulate cortex are involved in self-generated action and self-reflection (Passingham et al., 2010) in conjunction with parietal regions (precuneus, inferior parietal cortex) and sub-cortical structures (Boecker et al., 2008).

We think that the results we present may support usefulness of tDCS in clinical practice and particularly in cerebrovascular disease recovery (Liendeberg et al., 2010). Indeed, after a cortical motor stroke homo- and contralateral sensory cortices, ipsilateral basal ganglia, thalamus and cerebellum and remote brain areas, functionally connected to the damaged motor cortex, display a depressed activity (Carmichael et al., 2004). This dysfunction may correlate with a worse outcome in the subacute phase of stroke (Takasawa et al., 2002). As we have shown AtDCS, by increasing and thus strengthening synaptic connections among functionally related areas in the motor cortical network, might improve both the motor recovery and the outcome.

CONCLUSION

Combining tDCS with high-density EEG allowed us to evidence after effects of tDCS dependent on the polarity of the stimulation. We documented changes of cortical oscillatory activity over the stimulated primary motor area as well as in distant functionally related regions.

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