Brain Stimulation (2012) 5, 454–61

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ORIGINAL ARTICLES

Bifrontal and bioccipital transcranial direct current stimulation (tDCS) does not induce mood changes in healthy volunteers: A placebo controlled study

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Transcranial direct current stimulation (tDCS) is the application of a weak electrical direct current (1.5 mA), which has the ability to modulate spontaneous firing rates of the cortical neurons by depolarizing or hyperpolarizing the neural resting membrane potential. tDCS in patients with depressive disorders has been proven to be an interesting therapeutic method potentially influencing pathologic mood states. Except one study, no alterations in mood could be confirmed applying tDCS in healthy participants. In this study, bifrontal or bioccipital stimulation was applied in 17 healthy subjects during 20 minutes with 1.5 mA in a placebo-controlled manner. Bifrontal stimulation consisted of both anodal and cathodal placement on right and left dorsolateral prefrontal cortex (DLPFC) in two separate sessions. Using a set of self-reported moodscales (SUDS, POMS-32, PANAS, BISBAS) no significant mood changes could be observed, neither with bifrontal nor bioccipital tDCS. As already demonstrated by previous studies, we confirmed the minimal side effects and the safety of this neuromodulation technique.

Keywords tDCS; bifrontal; bioccipital; healthy subjects; mood changes

The application of a direct current to the central nervous system, known as transcranial direct current stimulation (tDCS), is neither new nor unknown. In 1801, Giovanni Aldini, Galvani's nephew, tried to treat melancholy by using Galvanic current (= direct current) stimulation.[1] Animal research has shown that tDCS is capable of altering the membrane resting state potential leading to depolarization or hyperpolarization, based on the polarity of the electrode.[2,3] The direct current can pass the human skull as shown by recordings on intracerebral electrodes,[4] suggesting that it can modify the excitability of the human cerebral cortex. The effects of stimulation can be long-lasting and are determined by the duration and magnitude of the current application.[5,6] The effects can last up to 90 minutes after a stimulation of 13 minutes.[6]

Animal studies have demonstrated the development of brain lesions underlying the cathode caused by high intensity direct current stimulation and consequently safety margins in animals have been described.[7] The currents used in humans (1-2 mA, 25-30 cm^2 electrode, 20-30 minutes)

M.P. and K.J. made equal contributions to this study.

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Submitted January 18, 2011; revised July 12, 2011. Accepted for publication July 12, 2011.

1935-861X/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.brs.2011.07.005

are well below the currents required to induce lesions. Magnetic resonance imaging has verified this, and no arguments have been revealed for structural changes in the brain (edema, necrosis) caused by direct current stimulation.[8] Electrophysiologic adverse effects have been ruled out as well.[9]

Possible side effects of tDCS are usually transient and mild. They consist of a transient itching or tingling sensation underneath the electrode, and headache and fatigue are the most profound ones.[10] Local burns at the side of the anode can occur when high amplitudes are used with insufficient moisturizing at the electrode site.[11] Because the induced paresthesias are transient, tDCS is a good tool to use in randomized controlled trials with a sham study arm.[12]

The first 20th century study describing mood changes by tDCS in humans, including three healthy participants and 29 patients with a mental disorder, was performed in the early sixties[13]; whereas anodal (+ electrode) stimulation resulted in increased cheerfulness, alertness, and talkativeness, cathodal (− electrode) stimulation resulted in quietness and apathy. However, except one study, these results were not replicated in later studies with healthy subjects applying bifrontal or bioccipital stimulation.[14,15] The only study confirming mood effects of frontal stimulation in healthy subjects was reported by Marshall et al.[16] who applied intermittent tDCS during sleep and wakefullness.

Recently a revival in research with tDCS is noted for the treatment of mood disorders, indicating that direct current stimulation can be beneficial as a treatment for patients with a major depression.[17-20] In addition to mood alterations, tDCS has the potential to affect memory,[16] visual perception[21] and the somatosensory system, including pain,[22-25] as well as motor function[18,26,27,28] and cognitive processes.[29-31] In this study we wanted to take the possible asymmetry between left and right prefrontal activity described in depression and anxiety disorders into account,[32] more specificly at the dorsolateral prefrontal cortex (DLPFC) areas.[33] The DLPFC is part of a larger network implicated in depression consisting of the amygdala, thalamus, and basal ganglia as well as the subgenual, and dorsal anterior cingulate cortex, insula, and other prefrontal areas,[34-39] analogous to the network described for dysthymia, a more common (6% prevalence) but less severe chronic mood disorder.[40] Hence, we used a bifrontal stimulation design in which the cathode and anode were simultaniously positioned at the DLPFC, respectively at the right and left side (F3 and F4 of the 10/20 International System).

Besides the bifrontal stimulation we implemented another location for the tDCS electrodes, namely, at the occipital area, which is covered by the greater occipital nerve, a branch of the C2 nerve. The rationale was based on a publication by Thimineur et al.[41] In this study 12 patients, having fibromyalgia, were implanted with an occipital nerve stimulator at the level of the greater occipital nerve (C2).[41] The patients experienced an improvement in pain scores and additional positive effects on their mood and fatigue. This might, of course, be correlated with the decrease in pain scores, but it could also be an independent effect caused by the stimulation.

Consequently, we hypothesized that tDCS may alter the excitability of the greater occipital nerve by its capability of altering the excitability of peripheral nerves.[42] However, occipital tDCS might act on mood via another mechanism as well. A $^{15}H_2O$ PET-scan study revealed activity changes in remote brain structures, besides the focal effects underneath the electrode.[43] This might be related to the existence of structural long-range connections in the brain. One of the most robust connections exists between the frontal and occipital brain areas.[44] Based on this connectivity, as well as the diffuse effects of tDCS, we hypothesized that bioccipital tDCS might influence mood-related structures. The main goal of this study was to evaluate mood and behavioral effects of tDCS in a very homogeneous group of healthy volunteers. A design in which each patient received six different types of stimulation was elected, including: three sessions of bifrontal stimulation (left sided, right sided, and sham stimulation) and three sessions of bioccipital stimulation (left sided, right sided, and sham stimulation). The current study design has the advantage of exploring tDCS-induced mood alterations related to different stimulation sites inclusive of potential lateralization effects. In addition, participants were consequently asked about possible side effects immediately after each session and before each subsequent one to objectivate the safety of this neuromodulation technique.

Methods

Participants

Participants for this study were recruited among medical students at the University of Antwerp, Belgium. Written advertisements were posted around the campus with contact information of the investigators. The interested students could contact the investigators and were given all the necessary explanation concerning the purpose and risks of the study. Volunteers were screened by a physician and excluded from participation when necessary, in compliance with the following criteria: (1) age between 21 and 25 years, (2) male sex, (3) not having significant physical or mental ilness, (4) no history of substance abuse, (5) no history of epileptic insults, and (6) drug free. Seventeen healthy, drug-free male participants were included in the study (age 21.47 ± 0.91 years). None of the volunteers ever participated in studies using tDCS, TMS, or other forms of neuromodulation. This study was approved by the Ethical Committee of the University Hospital Antwerp, Belgium. All volunteers gave written informed consent. No financial compensation was given. The purpose and design of the study was clear to all participants.

Study design

The study was designed as a single-center, randomized placebo-controlled cross-over study. After enrollment and giving informed consent, participants were randomized in a counter-balanced manner into three study arms for bifrontal stimulation and subsequently into three study arms for bioccipital stimulation. For both stimulation localizations the trial existed out of three similar stimulation conditions: (1) left cathodal/right anodal stimulation, (2) right cathodal/left anodal stimulation and (3) sham stimulation. The participants and investigator were blinded for the tDCS conditions. tDCS was applied by a staff member at the department, who was aware of the stimulation condition, but had no other involvement in the study procedure. All participants completed the three different forms of bifrontal stimulation, 16 of 17 participants completed all three forms of bioccipital stimulation. One participant stepped out of the study protocol after his fourth stimulation, because of personal reasons, interfering with the time schedule of the study.

Stimulation procedures

The participants underwent three sessions of bifrontal stimulation (cathode left/anode right, cathode right/anode left, and sham stimulation) and three sessions of bioccipital stimulation (cathode left/anode right, cathode left/anode right, and sham stimulation) with a minimum time interval of 24 hours between each session. Bipolar tDCS was delivered by a battery-driven stimulator (Mind Alive Inc., Edmonton, Alberta, Canada), with two conductive-rubber electrodes, placed in saline-soaked sponges (5×7 cm). For the bifrontal stimulation sets, the electrodes were positioned over the left and right DLPFC, consistent with electrode coordinates F3 and F4 in the 10/20 International System. For the bioccipital stimulation sets the electrodes were positioned over the left and right occipital area, 2 cm lateral of the inion, consistent with electrode coordinates O1 and O2 in the 10/20 International System. The placement of the cathode and anode of the tDCS depended on the above mentioned randomization. For the sham condition, the cathode was placed at the left side and the anode at the right side at the frontal or occipital area respectively. Skin resistance was reduced during stimulation by applying saline.

Real tDCS consisted of a current of 1.5 mA for 20 minutes, with stimulation current ramped up during the first 10 seconds of stimulation.

During sham stimulation the electrodes were placed bifrontally or bioccipitally, respecting the randomization. The direct current was delivered for 10 seconds, with the same ramp up as during real stimulation. Afterward the device was turned off. Sham tDCS lasted for 10 seconds, the device was kept out of sight of the participant to keep the participant blinded. This sham procedure has shown to be feasible.[12]

Ouctome parameters

In this study we wanted to evaluate the effects of bifrontal and bioccipital tDCS on mood and behavior.

To evaluate mood changes, a set of self-reported moodscales consisting of Subjective Units of Distress (SUDS), shortened Profile of Mood States (POMS-32), and the Positive Affect and Negative Affect Schedule (PANAS) was used. To evaluate subjective changes in behavioral activity the Behavioral Approach System and Behavioral Inhibition System (BISBAS) was chosen. The acquisition of these parameters was performed directly prestimulation (baseline) and directly after each of the six stimulation sessions. After each stimulation session and before each subsequent one, the participants were questioned for possible sensations and adverse effects accompanying or following direct current stimulation to evaluate the safety and invasiveness of this modulation technique.

Subjective units of distress (SUDS)

All partipants were asked to score their subjectively experienced distress between 0 (meaning no distress) and 10 (meaning maximal distress).

Dutch shortened profile of mood states (POMS-32)

The shortened version of the profile of mood states consists of 32 items of mood desciptors (e.g., sad) and is based on the profile of mood states (POMS).[45] The items are rated on a five-point scale starting from 0 indicating a low level ("not at all") up to 4 indicating a high level ("extremely") to evaluate the current feelings. It measures five covarying mood-factors (depression-rejection, anger-hostility, fatigue-inertia, vigor-activity, and tension-anxiety).

Positive affect and negative affect schedule (PANAS)

The positive affect and negative affect schedule (PANAS) is a 20-item inventory that assesses two emotional dimensions, i.e., positive mood (10 items) and negative mood (10 items).[46] The items are rated on a five-point scale, with a rating of 1 indicating a low level ("very slightly or not at all") and a rating of 5 indicating a high level ("extremely") of a given mood.

Behavioral inhibition system–behavioral approach system (BISBAS)

A behavioral approach system (BAS) is believed to regulate appetitive motives, in which the goal is to move toward

something desired. A behavioral avoidance (or inhibition) system (BIS) is said to regulate aversive motives, in which the goal is to move away from something unpleasant.[47] Each question of the 24-item questionnaire is rated on a four-point scale with 1 indicating a high level ("very true for me") and 4 indicating a low level ("very false for me"). BIS consists of seven items, BAS of 13. BAS can be split-up in three covarying factors: BAS Drive (four items), BAS Fun Seeking (four items), and BAS Reward Responsiveness (five items). Four items of the BISBAS are fillers.

Statistical analysis

All results were analyzed using the SPSS statistical software for windows (version 15.0, SPSS, Inc., Chicago, IL). Before analyzing the data, self-reported change percentages were calculated. To calculate these percentages the prestimulation scores were subtracted from the poststimulation scores divided by the prestimulation scores. To test the effect of stimulation condition on the self-reported change percentages, a repeated measure analysis of variance (ANOVA) was conducted for respectively the three sessions (sham, anodal, and cathodal) of bifrontal and bioccipital tDCS. We used a Bonferroni correction for multiple comparisons when the results obtained significance. An additional analysis was performed to verify whether the obtained results survive multiple comparisons when correcting for the different tests using a multivariate repeated measure ANOVA including the three sessions for all separate tests in one analysis for respectively bifrontal and bioccipital tDCS.

Results

Descriptives

All 17 participants initially enrolled in the study completed the three bifrontal stimulation sets. Sixteen of 17 participants completed the three bioccipital stimulation sets. All the acquired data were entered in the analysis of the group data. Table 1 shows the mean baseline scores and standard deviations.

Observational

The blinded experimenter did not notice any significant changes in mood or fatigue. During onset of the stimulation subjects experienced a tingling or burning sensation at the site of the electrodes. One subject reported nausea during stimulation; however, this was during sham stimulation and disappeared within 1 hour, without medical interference.

Frontal tDCS

The analyses yielded no significant effects for the SUDS, BIS, PANAS, and POMS. Yet, a significant effect was obtained for BAS ($F(2,15) = 4.33$, $P = 0.03$). Further analysis revealed that this effect could mainly be explained because of the subscale BAS FUN ($F(2,15) = 12.48$, $P = 0.001$). A pairwise comparison revealed that for BAS FUN there was a difference between cathode left/anode right and the sham session; however, there was no difference with the cathode right/anode left condition (which on itself did not differ significantly from sham stimulation). Both effects disappeared, however, when corrected for multiple comparisons over the different tests. An overview of the results is given in Table 2.

Table 1 Mean scores (M) and standard deviations (SD) for the baseline measurements for the SUDS, BISBAS, PANAS, and POMS

	Baseline	
	M	SD
SUDS	2.76	1.92
BIS	15.41	3.33
BAS	22.78	4.71
BAS Drive	7.18	2.04
BAS Fun Seeking	7.41	2.43
BAS Reward Responsiveness	8.06	1.92
PANAS		
Negative affect	3.71	3.57
Positive affect	19.70	5.90
POMS		
Depression	1.76	3.41
Fatigue	6.43	5.62
Tension	3.23	2.14
Anger	1.14	1.76
Vigor	13.74	7.00

Bioccipital tDCS

No significant results were obtained for the SUDS, BIS BAS, negative affect of the PANAS, and the POMS. However, the analyses yielded a significant effect for the positive affect subscale of the PANAS ($F(2,14) = 3.93$, $P = 0.04$). A pairwise comparison revealed that there was a difference between the cathode left/anode right condition and the sham session for positive affect. However, there is no significant difference with the cathode right/anode left condition (which on itself did not differ significantly from sham stimulation). This effect disappeared when it was corrected for multiple comparisons over the different tests. An overview of the results is given in Table 3.

Discussion

Neither with bifrontal stimulation, nor with bioccipital stimulation any profound alteration in mood or behavior was demonstrated for both conditions (cathode left/anode right versus cathode right/anode left). On the basis of the

Table 2 Mean change percentages and standard deviation for the SUDS, BISBAS, PANAS, and POMS for frontal tDCS

Stimulation condition	Sham	Cathodal r Anodal l	Cathodal l Anodal r	*F* (2,15)	*P*
SUDS	−27.94 (−0.29)	−30.88 (−25.17)	−22.06 (−21.17)	1.12	0.35
BIS	−2.75 (−8.41)	−11.00 (8.89)	35.73 (26.84)	2.08	0.16
BAS	−11.45[a] (−9.22)	−1.60[a,b] (2.18)	4.03[b] (8.62)	4.33	0.03
BAS Drive	−1.31 (1.38)	−1.96 (−0.77)	1.31 (2.69)	1.19	0.33
BAS Fun Seeking	−4.07[a] (−3.41)	0.45[a,b] (1.0)	1.36[b] (1.89)	12.48	0.001
BAS Reward Responsiveness	−9.80 (−5.48)	0.00 (2.45)	0.00 (7.35)	0.88	0.44
PANAS					
Negative affect	−29.41 (−25.26)	−34.11 (−30.24)	−49.41 (46.44)	1.54	0.25
Positive affect	3.36 (5.24)	9.66 (12.33)	−6.72 (−5.02)	0.73	0.50
POMS					
Depression	−4.28 (−3.10)	−4.99 (−3.86)	−13.55 (−12.92)	0.60	0.56
Fatigue	−17.21 (−13.63)	−34.45 (−33.03)	−42.49 (−41.54)	0.93	0.42
Tension	−35.29 (−31.48)	−36.76 (−33.05)	−45.59 (−43.86)	0.28	0.76
Anger	8.65 (9.16)	−2.87 (−3.04)	−7.67 (−8.12)	1.06	0.37
Vigor	22.66 (20.50)	12.20 (11.18)	−1.74 (−3.59)	0.33	0.72

The obtained significant effects did not survive correction for multiple comparisons over the different test.
[a,b] Significant differences between sessions (Bonferroni correction for multiple comparison).

findings of this study, tDCS did not seem to be capable of affecting mood in healthy male subjects.

These results are in line with a publication from 1968 on tDCS and mood changes in healthy subjects that revealed no significant results.[48] A more recent publication by Koenigs et al.[25] reported similar findings. In this study, a current of 2.5 mA was delivered for 35 minutes in 21 healthy participants with bifrontal electrodes placed at the level of the orbitofrontal cortex (OFC) and one extracephalic electrode on the nondominant arm. They used the POMS as an outcome parameter to observe variation in mood, but statistical analysis yielded no significant results.

Another recent publication in healthy participants applied anodal stimulation of the left DLPFC and stated that this electrode positioning has the ability of reducing the perception of pain unpleasantness and emotional discomfort that accompanies the presentation of aversive pictures.[14] Despite these interesting results, the study did not evaluate the alterations in general mood state or behavior. But it has to be noted that the stimulation with an intensity of 2.0 mA was only applied during 5 minutes. Apart from bifrontal stimulation, anodal occipital stimulation was applied as well, but no significant effect could be detected in reducing pain unpleasantness or discomfort nor in alteration of general mood.

Table 3 Mean change percentages and standard deviation for the SUDS, BISBAS, PANAS, and POMS for bioccipital tDCS

Stimulation condition	Sham	Cathodal r Anodal l	Cathodal l Anodal r	*F* (2,14)	*P*
SUDS	−19.11 (14.36)	−6.25 (−1.95)	−3.13 (1.36)	1.96	0.13
BIS	−32.99 (−40.42)	−17.52 (24.46)	−20.44 (−27.56)	2.11	0.16
BAS	−0.32 (−3.24)	−5.13 (−0.65)	2.05 (5.27)	0.65	0.54
BAS Drive	0.65 (1.35)	2.08 (2.90)	3.47 (4.38)	0.72	0.50
BAS Fun Seeking	0.45 (0.93)	−2.40 (−1.11)	−0.48 (−0.03)	0.51	0.61
BAS Reward Responsiveness	−4.90 (−0.29)	−13.02 (−8.63)	−5.21 (−0.33)	0.47	0.64
PANAS					
Negative affect	−27.06 (−22.77)	−17.50 (−12.34)	−26.25 (−21.64)	0.05	0.95
Positive affect	2.52[a] (4.35)	−10.71[a,b] (−6.92)	−15.18[b] (−13.45)	3.93	0.04
POMS					
Depression	−6.42 (−5.37)	6.06 (7.95)	−2.27 (−0.90)	2.21	0.15
Fatigue	−17.23 (−14.79)	−26.82 (−26.05)	−24.40 (−21.04)	0.69	0.52
Tension	−48.53 (−45.50)	−32.81 (28.61)	−40.63 (−36.91)	0.43	0.66
Anger	0.97 (1.02)	8.18 (8.69)	19.39 (20.60)	1.95	0.18
Vigor	0 (−3.49)	12.96 (17.48)	−1.85 (−7.52)	0.12	0.89

The obtained significant effects did not survive correction for multiple comparisons over the different test.
[a,b] Significant differences between sessions (Bonferroni correction for multiple comparison).

The only significant improvement in mood induced by tDCS in healthy participants was described by Marshall et al.[16] The stimulation design consisted of the application of two frontal anodes (F3 and F4 of the International 10/20 System) and two cathodes placed over the mastoid. In contrast to the previously mentioned studies, stimulation was applied intermittently (15 seconds on and 15 seconds off) with a current density of 0.26 mA/cm^2 during sleep and wakefulness. Compared with sham stimulation, a significant decrease in depressive feelings was noted by the Eigenschaftswörterliste (EWL), a checklist describing a subject's mood in 15 dimensions, as well as an improvement of mood using the PANAS. Although significant alterations in mood could be detected, the stimulation procedure was obviously different to the previously mentioned studies (electrode placement, intermittent stimulation). This study protocol only included male participants, similar to the current study. This could be an interesting notion, because it has been assumed that the efficacy of tDCS is influenced by gender.[49,50]

In contrast to the absent or limited findings in recent studies applying tDCS in healthy participants, remarkable effects were obtained by the above mentioned study by Lippold et al.[13] in 1964. In the healthy subjects Lippold's cathodal (−) stimulation lead to quietness in two of three subjects and to nausea and palor in the third subject. This third subject was stimulated at 3 mA, which aggravated the pain sensation of an already existing renal pain. Anodal (+) stimulation was performed in two of three subjects, from which one did not respond at all and from which the second subject showed increased alertness. In contrast to the absence of mood altering effects in healthy subjects, recent research has demonstrated that frontal direct current stimulation can provide as a treatment for patients with pathologic mood states, such as a major depression.[17-20] In other words, frontal tDCS might not exert an effect on normal mood, but only in pathologic mood states. In contrast to frontal tDCS, occipital stimulation could not induce any significant alteration of mood in patients with a major depressive disorder.[19]

The observations of Lippold et al.[13] and recently published results suggest that tDCS induced mood changes seem to be more profound in populations with pathologic mood states than in subjects with normal mood. In other brain stimulation approaches similar results are obtained. TMS tends to have more pronounced effects for mood alteration in populations with pathologic mood states, compared with healthy populations. High-frequency TMS of the left DLPFC and low-frequency TMS of the right DLPFC have shown to be effective in the treatment of patients having clinical depression,[51,52] hence changing pathologic mood. In studies involving healthy volunteers, results in mood changes are inconclusive. This counts for high frequency TMS on the left DLPFC[53,54] and low frequency of the right DLPFC.[55,56] A recent study applying repetitive transcranial magnetic stimulation (rTMS) in combination with affective priming also failed to reveal significant mood changes in healthy subjects using the affective go-no go task or visual analogue scale (VAS).[57] This study design was based on the observation that an activated brain region can facilitate the effect of TMS.[57] Even though no significant effects were found, this hypothesis could be a contributing factor to explain why neuromodulation techniques have more pronounced effects in pathologic mood states, in which brain activity is different from subjects without any mental disorder. Hypothetically, a more balanced and stable activity of the brain in healthy subjects might be more difficult to modulate.

The efficient therapeutic effects of TMS in depressive disorders by stimulating the left DLPFC or inhibiting the right DLPFC was one of the main motivations to explore the laterality of tDCS. Without the use of an extracephalic electrode, anodal and cathodal stimulation would be simultaneously active at the the opposite hemispheres, resulting in excitation of one hemisphere and inhibition of the other at the same moment. This kind of stimulation should accentuate the possible presence of lateralized brain activity associated with mood, but this hypothesis could not be proven by the current study.

An essential remark that has to be noted is, that despite the promising results of TMS in the treatment of depressive disorders, a limited respons rate of 50% has been observed among various studies.[58] Genetic polymorphisms are reported to be an important factor influencing the capacity to respond to TMS[59,60] and these interindividual patient characteristics can also be a significant predictor for tDCS efficacy in healthy subjects.[61]

The current study confirmed the inability of bioccipital tDCS to provoke effects on mood in healthy subjects[14] as has also been shown in major depression.[19]

Safety

Using tDCS in healthy subjects requires it to be a safe technique with minimal side effects. Different studies investigated the safety of tDCS in healthy subjects and patients. They all concluded that tDCS only provokes mild side effects, when current stimulation guidelines (1-2 mA, 25-30 cm^2 electrode, 20-30 minutes) were respected.

The side effects most often reported were a mild tingling and itching sensation at the side of stimulation electrodes, except for a moderate fatigue and headache.[10] An important caveat is that these sensations were also reported during placebo stimulation, in which electrical current was turned off after 30 seconds in one study.[12] In line with these observations, the participants of this study did not declare any serious side effects, except for a tingling feeling at the side of the stimulation electrode.

Limitations

Although our results are similar to other recent studies, some important remarks should be made.

1. The time interval between different stimulation procedures varied inter- and intraindividually, but always comprised minimal 24 hours to exclude carry-over effects.
2. Side effects were observed and inquired routinely, but were not systematically assessed by a written questionnaire.
3. The self-reporting mood scales that were used may lack the sensitivity to identify limited changes in normal mood. To detect even small changes in mood states, the use of multiple questionnaires, with a high sensitivity might be interesting.[62]

Conclusion

In this study we attempted to change mood in healthy subjects by using bifrontal and bioccipital tDCS with simultaneous stimulation of the right and left hemisphere with anodal and cathodal stimulation, respectively. This design provided no profound changes in mood.

Four reasons can be proposed for these negative findings in contrast to previous studies: (1) stimulation design differences (stimulation location, duration, electrode size), (2) participant characteristics (healthy versus psychiatric clinical populations), (3) interindividual differences in respons to tDCS, and (4) the lack of an appropriate instrument to measure outcome.

This study confirms the safety of bilateral frontal and occipital tDCS.

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