Facilitation of visuo-motor learning by transcranial direct current stimulation of the motor and extrastriate visual areas in humans

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Abstract

Performance of visuo-motor tasks requires the transfer of visual data to motor performance and depends highly on visual perception and cognitive processing, mainly during the learning phase. The primary aim of this study was to determine if the human middle temporal (MT)+/V5, an extrastriate visual area that is known to mediate motion processing, and the primary motor cortex are involved in learning of visuo-motor coordination tasks. To pursue this, we increased or decreased MT+/V5, primary contralateral motor (M1) and primary visual cortex excitability by 10 min of anodal or cathodal transcranial direct current stimulation in healthy human subjects during the learning phase of a visually guided tracking task. The percentage of correct tracking movements increased significantly in the early learning phase during anodal stimulation, but only when the left V5 or M1 was stimulated. Cathodal stimulation had no significant effect. Also, stimulation of the primary visual cortex was not effective for this kind of task. Our data suggest that the areas V5 and M1 are involved in the early phase of learning of visuo-motor coordination.

Introduction

The middle temporal (MT) and medial superior temporal cortical areas of the monkey brain and the homologous region of the human cortex, MT+ or V5, are active during passive visual perceptual tracking of motion (Culham *et al*., 1998) and during active manual tracking movements (Kleiser *et al*., 2002; Kruse *et al*., 2002). While these cortical areas are centrally involved in motion perception, the role of these cortices in visuo-motor learning is less clear, particularly in view of the many active brain areas in these processes, including the primary motor cortex, pre-motor and supplementary motor areas, the parietal cortex, the basal ganglia and the cerebellum (Pascual-Leone *et al*., 1994; Grafton *et al*., 2001; Balslev *et al*., 2002). Imaging studies and electroencephalographic measurements imply a crucial role of the cortico-striatal system in learning new visuo-motor associations (Staines *et al*., 2002; Toni *et al*., 2002). Additionally, transcranial magnetic stimulation studies revealed the importance of the parietal cortex in visuo-motor learning (Walsh *et al*., 1998a, 1999; Ellison *et al*., 2003). Nevertheless, the role of V5, an extrastriate area in which neurons are broadly tuned to identify the direction and velocity of visual motion, remains partly in doubt during the acquisition of a visuo-motor task.

Changes of neuronal activity and excitability accompany the learning of new skills. The idea of manipulating cortical excitability externally to improve learning processes is not new. So far it has been demonstrated in neuropharmacological investigations that excitability-enhancing pharmacological agents, such as amphetamine,

improve use-dependent plasticity (Bütefisch *et al*., 2002), while γ-aminobutyric acid agonists diminish it (Blin *et al*., 2001). Transcranial direct current stimulation (tDCS) is a non-invasive stimulation method that offers the possibility to induce prolonged excitability changes in the cortex, as was found in several studies with animals (Creutzfeld *et al*., 1962; Bindman *et al*., 1964; Ward & Weiskrantz, 1969) and humans (Nitsche & Paulus, 2000, 2001; Antal *et al*., 2001, 2003, 2004a,b; Baudewig *et al*., 2001; Nitsche *et al*., 2003a,b). From previous animal studies it is known that cathodal tDCS reduces spontaneous firing rates of cortical cells, most likely by hyperpolarizing the cell body, while anodal stimulation results in a reverse effect (Creutzfeld *et al*., 1962; Bindman *et al*., 1964; Ward & Weiskrantz, 1969). In humans, tDCS modulated the amplitude of motor-evoked potentials in a polarity-dependent way: anodal stimulation increased the motor-evoked potentials amplitude while cathodal stimulation decreased it (Nitsche & Paulus, 2000). In the visual cortex, tDCS modified the amplitude of visual-evoked potentials (Antal *et al*., 2004a) and the perception of phosphenes (Antal *et al*., 2003) in a polarity-dependent way. The tDCS-induced effects outlast the stimulation itself and they are most probably localized intracortically (Nitsche & Paulus, 2001; Nitsche *et al*., 2003a,b). Recently, it was shown that the evoked after-effects are *N*-methyl-D-aspartate receptor dependent (Liebetanz *et al*., 2002; Nitsche *et al*., 2003c), and thus share some similarity with the long-term potentiation and depression presumed to underlie learning processes (Rioult-Pedotti *et al*., 2000). Thus, an excitability enhancement by anodal tDCS may improve visuo-motor learning.

Indeed, functional approaches revealed that anodal stimulation of the dorsolateral prefrontal cortex improved performance in a delayed reaction time task in monkeys, while cathodal stimulation resulted in
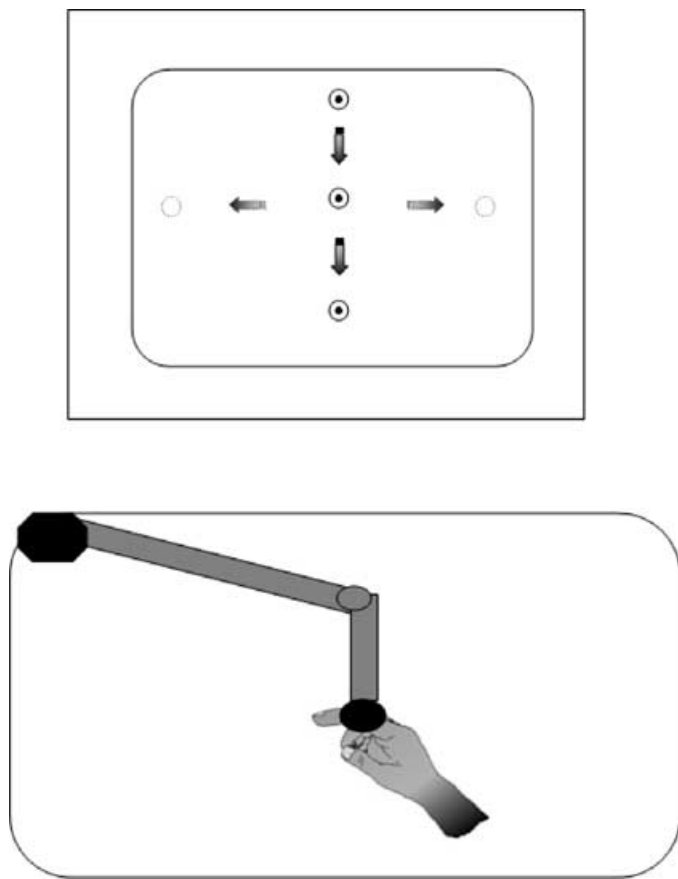
FIG. 1. The figure shows a sketch of the visuo-motor task we used. After the feedback cursor appeared in the middle of the screen, the target dot appeared in one of the four possible positions and moved towards the feedback cursor. When it reached the feedback cursor, the subject had to follow it with the feedback cursor by moving the manipulandum with the right hand, until it stopped. An error occurred if the feedback cursor left the tracking window before a trial was completed or it did not stop when the target stopped.

an impairment (Rosen & Stamm, 1972). tDCS also changed the performance in an avoidance-learning task (Albert, 1966), and anodal tDCS of the primary motor cortex improved implicit motor learning (Nitsche *et al.*, 2003a).

To determine if the external modulation of primarily motion-sensitive visual areas contributes to visuo-motor learning, anodal and cathodal tDCS were applied to the left V5 and additionally in different experimental sessions to the left primary motor cortex and the visual area (V1) during the learning phase of a visuo-motor coordination task. We used a visually guided manual tracking task in which movements of the hand on a horizontal plane were required in four directions with a moving 2D manipulandum and could also be seen on a monitor as a feedback cursor (Fig. 1). Previous primate and our human studies have suggested that this task requires dynamic interactions between visual input and movement (Kruse *et al.*, 2002; Antal *et al.*, 2004b). For a correct execution of this task, a combination of intact motion perception, integration and motor execution is needed. In the first part of the task only a correct perception of the target motion is necessary. In the second phase, when the target stimulus must be followed by the feedback cursor, a continuous, high-resolution evaluation of both the correct direction and speed of the motion according to the target-feedback cursor combination is necessary to choose the optimum motor reaction.

Materials and methods

Subjects

Forty-two healthy, right-handed subjects participated in the study (mean age: 25.5 years; range: 19–38 years; SD: 4.67, 15 men). Ten subjects took part in a no-stimulation condition, 14–14 subjects (seven subjects had cathodal, seven subjects anodal stimulation in each condition) in the V5 and primary contralateral motor (M1) stimulation, and four subjects (two cathodal and two anodal stimulations) in the V1 stimulation conditions. All of the subjects participated only once in the study. They all fulfilled the following conditions: visual acuity better than 0.9, no metallic implants, no prior history of any neurological or psychiatric disorders, drug abuse or alcoholism. The subjects were interviewed about their state of health and were not taking any medication at the time of the experiment. All of the subjects gave their written informed consent. We conform to the Declaration of Helsinki (1991, *BMJ*, 302, 1194), and the Ethics Committee of the University of Göttingen approved the study.

Experimental procedure

In the visuo-motor coordination task the subjects were seated 75 cm in front of a SONY Triniton colour high-resolution monitor at approximately eye level. Under the monitor, a horizontal, planar work surface was placed, on which a 2D, purpose-built, articulated manipulandum could be moved manually. The movement of the manipulandum on the surface was measured continuously and displayed in real time as a feedback red dot (feedback cursor) on the screen. After the feedback cursor was placed on the middle of the screen into a $1.5°$ diameter centre-hold window, a white target dot appeared on the upper, lower, right or left middle part of the screen and travelled toward the red feedback dot. Subjects were instructed to follow the white target dot after it reached the position of the feedback cursor and to stop when the target stopped on the opposite side of the screen (correct tracking movement). The direction of the tracking movement was always straight. An error occurred if the feedback cursor left the tracking window before a trial was completed or it did not stop when the target stopped. The size of the target and feedback dot was $0.8°$ and $1.0°$, while the diameter of the tracking window was $1.5°$. The tracking window could not be seen by the subjects. The pre-movement and tracking durations were both 1250 ms, the velocity of the target dot was $2.0°/s$. Tracking movements were recorded online. Before the initiation of the experimental session, a short introduction was given to make sure that the subject understood the task and the subjects had a practice session including 10–12 trials. Afterwards, 10-min cathodal or anodal tDCS was applied to one of the cortical areas (see below), and five blocks of 50 trials (altogether about 25 min) were performed with each subject. The stimulation was terminated exactly at the end of the second block.

tDCS stimulation

tDCS was delivered by a battery-driven constant DC current stimulator (Schneider Electronic, Gleichen, Germany) using a pair of electrodes in a 5×7-cm water-soaked synthetic sponge. Three different electrode configurations were used. (i) For V5 stimulation, one electrode was placed approximately 4 cm above the mastoid-inion line and 7 cm left to the midline in the sagittal plane. The other electrode was positioned over Cz. Polarity of the stimulation referred to the electrode placed over V5 (V5–Cz montage). The coordinates were selected on the basis of previous MRI and TMS studies of V5 (Watson *et al.*, 1993; Hotson *et al.*, 1994; Walsh *et al.*, 1998b; Hotson & Anand, 1999; Stewart *et al.*, 1999). Left V5 was stimulated because these studies suggest that TMS over the left V5 produces a greater disturbance in a visual motion task

than TMS over the right V5. PET studies also show a greater prominence of motion processing in the left hemisphere (Zeki *et al.*, 1991). (ii) For the motor cortex stimulation, one electrode was placed over the hand area of the left motor cortex (located by TMS) and the other over the right orbit (LM–RO montage). Polarity of stimulation referred to the electrode placed over LM. (iii) For the stimulation of the primary visual cortex, one electrode was placed at Oz, the other electrode over Cz (Oz–Cz montage). Polarity of stimulation referred to the electrode placed over Oz. The current was applied for 10 min with an intensity of 1.0 mA. Constant current flow was controlled by an ampere-meter.

The changes in number of correct tracking movements were entered into a 3 (no stimulation – anodal or cathodal stimulation) $\times$ 5 (time) analysis of variance (ANOVA) for each cortical area separately. Student's *t*-tests were used for post-hoc comparisons.

Results

All of the subjects were able to learn the tracking task. Using the V5–Cz electrode montage, anodal stimulation enhanced the relative number of correct tracking movements at the beginning of the learning process, whereas cathodal stimulation had no such effect. There was a significant main effect of stimulation ($F_{2,21} = 2.90$, $P < 0.05$) and time course ($F_{4,84} = 128.7$, $P < 0.0001$). The interaction between stimulation type and time course was not significant ($F_{8,84} = 1.5$, $P > 0.05$). According to the post-hoc test the number of correct trials increased significantly in the first block (about 0–5 min after the initiation of the stimulation) during anodal stimulation ($P < 0.05$) compared with the no-stimulation condition (Fig. 2).

Using the LM–RO montage, the main effect of stimulation was insignificant ($F_{2,21} = 0.9$, $P > 0.4$). The time course ($F_{4,84} = 90.75$, $P < 0.0001$) and the interactions between stimulation type and time course were significant ($F_{8,84} = 2.54$, $P < 0.05$). According to the post-hoc test, the number of correct trials increased significantly in the first block (about 0–5 min time interval after the initiation of the stimulation) during anodal stimulation ($P < 0.05$) compared with the no-stimulation condition (Fig. 3).

In the Oz–Cz montage, four subjects were involved. Anodal and cathodal stimulations showed no differences between the stimulation
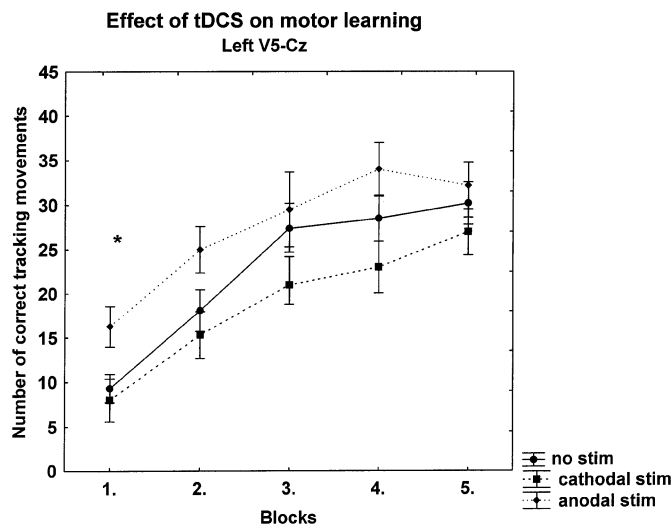

FIG. 3. Effect of transcranial direct current stimulation (tDCS) on tracking performance when the left M1 was stimulated. Error bars show SEMs. Anodal tDCS significantly improved performance in the 0–5 min interval of stimulation.

conditions ($P > 0.1$). The number of errors did also not differ between stimulation conditions (Fig. 4).

Discussion

The main finding of our study is that an excitability enhancement of V5 and M1 induced by anodal tDCS improved performance in the early phase of learning in a visuo-motor coordination task. These data suggest that V5, which is known to be important in high-resolution movement direction identification, in conjunction with M1, is involved in the learning of manual tracking movements. In contrast, the stimulation of the primary visual cortex did not result in significant changes in visuo-motor performance.

The importance of cortical V5 and its adjacent areas in the normal perception of moving stimuli has been well established by several

FIG. 2. Effect of transcranial direct current stimulation (tDCS) on tracking performance when the left V5 was stimulated. Error bars show SEMs. Anodal tDCS significantly improved performance in the initial phase of stimulation.
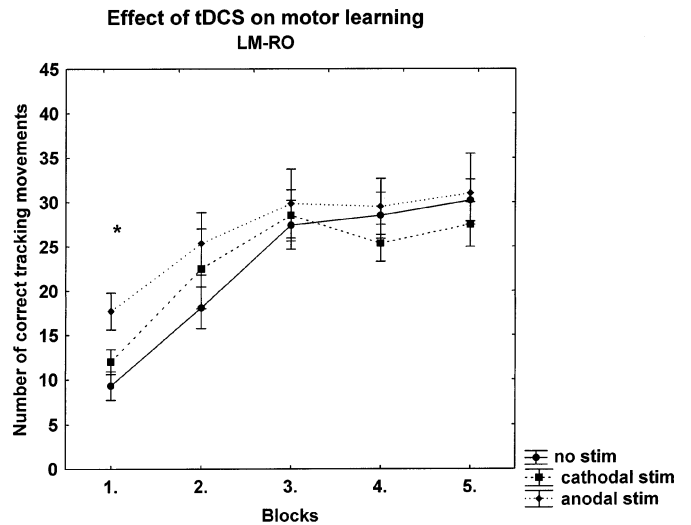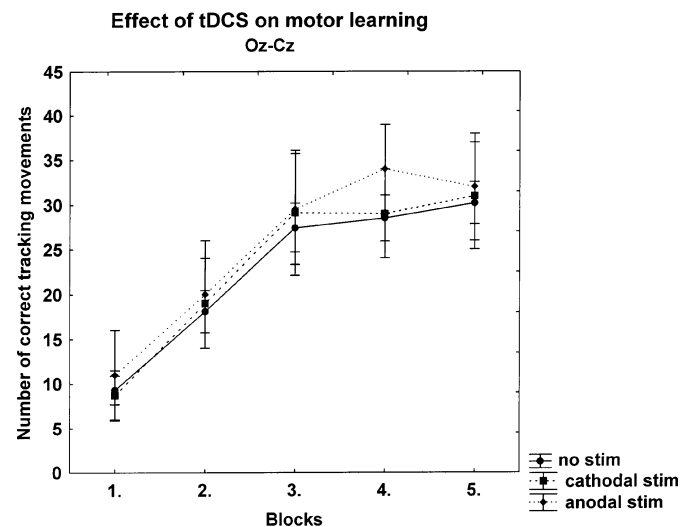

FIG. 4. Effect of transcranial direct current stimulation (tDCS) on tracking performance when the primary visual cortex was stimulated. Error bars show SEMs.

studies (for a review, see: Stewart *et al.*, 1999). Its location on the ventrolateral surface of the brain makes it particularly accessible in studies using external stimulation techniques. Several studies found that TMS of this area impaired performance in visual motion tasks (Beckers & Hömberg, 1992; Hotson *et al.*, 1994; Beckers & Zeki, 1995; Walsh *et al.*, 1998b; Stewart *et al.*, 1999; Campana *et al.*, 2002). Stewart *et al.* (1999) reported that stimulation of V5 changed learning of a visual motion task in a frequency-specific manner: subjects who were stimulated with 3 Hz frequency over the left V5 learned significantly less during a 4-day session than the control group or the group receiving 10 Hz stimulation. However, the specific function of V5 in visuo-motor learning is not clear so far. Here it is shown that an external excitability enhancement by anodal tDCS improved the acquisition phase of learning.

Anodal stimulation of M1 also resulted in increased performance at the beginning of the learning phase. It is largely agreed that M1 is involved in motor learning, as was shown by several fMRI and TMS studies: M1 shows enhanced activity and excitability, for example during learning of finger movements (Grafton *et al.*, 1992; Pascual-Leone *et al.*, 1994; Honda *et al.*, 1998). Recently it has been observed that an excitability change of M1 by repetitive TMS in a procedural motor learning task (Müllbacher *et al.*, 2002) or by tDCS in an implicit motor learning task (Nitsche *et al.*, 2003b) modulates motor learning specifically in the acquisition phase of the learning process.

In contrast to the previous findings, stimulation of V1 did not result in any effect on visuo-motor learning, suggesting that V1 is not critically involved in the learning process. This result shows also that stimulation of the vertex (Cz), which was a reference electrode in V5 and also in V1 stimulation conditions, could not be responsible for the initial learning process, while only the V5–Cz montage resulted in changes using this task.

In our study, the effect of anodal stimulation on learning was short-lived: learning was improved significantly only in the initial phase of the task, for 0–5 min after the beginning of anodal stimulation. One possible explanation could be that the initial phase of visuo-motor learning is the most sensitive for external modification, and that later the resulting sensory-motor coupling is so strong that it cannot be modified using this stimulation protocol. Otherwise, it is possible that these cortical areas are involved only in the initial phase of learning and other cortical areas, for example the parietal cortex (Müller *et al.*, 2002), are responsible for the later phases of the learning process. These areas were not stimulated in the present study. A third explanation could be that anodal stimulation did not improve learning but perceptual-motor performance by enhancing cortical excitability. It was suggested that improved psychophysical performance can result directly from increased neuronal sensitivity within a sensory pathway (Zohary *et al.*, 1994). Starting an over-learned motion discrimination task, a short-term increase of neuronal sensitivity of directionally selective neurons in MT of rhesus monkeys mirrored the increase in perceptual sensitivity, both in magnitude and time course. Accordingly, increasing the excitability of V5 and M1 neurons by anodal stimulation could have made them more sensitive to neuronal inputs, resulting in improved signal-to-noise ratio and improved performance accuracy. However, this explanation also has limitations: first, an unspecific increase of performance by enhanced excitability should be stable throughout the experiment; secondly, it should be independent of the stage of learning. Interestingly, in a previous study, using the same paradigm we demonstrated that cathodal stimulation of the left V5 improved visuo-motor performance when the task was over-learned (Antal *et al.*, 2004b). Based on research knowledge at present and the results of this study, definite conclusions cannot yet be drawn about which of the above-mentioned mechanisms plays the dominant role in the observed early performance increment.

Interestingly, V5 as well as M1 stimulations increased performance. Possibly this is due to the fact that both areas are involved in the early learning phases of visuo-motor coordination independently. Alternatively, visuo-motor information processing involves a transformation of the visual signal-to-noise ratio to motor areas, so that increasing this ratio in both areas by anodal tDCS could improve performance. Future experiments have to clarify this alternative mechanism.

Previous visuo-motor studies have focused mainly on the motor, parietal areas and the fronto-striatal connections during learning processes (Pascual-Leone, 1994; Walsh *et al.*, 1998a, 1999; Grafton *et al.*, 2001; Balslev *et al.*, 2002; Toni *et al.*, 2002; Ellison *et al.*, 2003). To our knowledge, this is the first study in the human showing that V5 is specifically involved in the learning of identification and selection of correct tracking movements. However, we also have to consider that modulation of the excitability of a given brain area is unlikely to affect neuronal function only in that targeted brain region. When activity of a given brain area is modified, the behavioural impact is the consequence of how the rest of the brain copes with the modulation of the activity. Our study also shows that excitability modulation in a neuronal network of V1, M1, V5 leads to changes in brain activity that can influence behaviour in different ways.

Acknowledgements

Abbreviations

M1, primary contralateral motor; MT, middle temporal; tDCS, transcranial direct current stimulation.

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