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The influence of theta transcranial alternating current stimulation (tACS) on working memory storage and processing functions

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The study aimed to explore the role of the fronto-parietal brain network in working memory function—in temporary storage and manipulation of information. In a single blind sham controlled experiment 36 respondents solved different working memory tasks after theta transcranial alternating current stimulation (tACS) was applied to left frontal, left parietal and right parietal areas. Both verum tACS protocols stimulating parietal brain areas (target electrodes positioned at location P3, or P4) had a positive effect on WM storage capacity as compared with sham tACS, whereas no such influence was observed for the stimulation of the left frontal area (target electrode positioned at location F3). A second finding was that left parietal theta tACS had a more pronounced influence on backward recall than on forward recall, which was not related to task content (spatial or verbal). The influence of theta tACS on WM executive processes was most pronounced for right parietal stimulation. The results are discussed in the broad theoretical framework of the multicomponent model of working memory.

1. Introduction

The psychological construct of working memory (WM) refers to a system that temporary holds or manipulates information we have just experienced, or retrieved from long-term memory (Cowan, 2001; Miyake & Shah, 1999). The majority of WM definitions encompass both, storage and processing components which are also integrated in the two most accepted models of WM —Baddeley's multiple-component system (Baddeley, Allen, & Hitch, 2011; Baddeley and Hitch, 1974), and Cowan's embedded processes model (Cowan, 2001, 2011).

From the neuropsychological perspective, the fronto-parietal network has been associated with working memory tasks (e.g., Chein & Fiez, 2010; Jonides et al., 2008; Palva, Monto, Kulashekhar, & Palva, 2010; Posner, 1990). It has been further suggested that the central executive function of WM is linked to frontal lobes whereas the WM storage component is associated with parietal areas (Champod & Petrides, 2010; Collette & Van der Linden, 2002; Olson & Berryhill, 2009; Sauseng, Griesmayr, Freunberger, & Klimesch, 2010). Based on the evidence from several brain imaging studies (Cowan, 2011; Cowan et al., 2011; Majerus et al., 2006, 2010; Todd & Marois, 2004; Xu & Chun, 2006), the left intraparietal sulcus (LIS) has been identified as unique for amodal or multimodal storage of information. Support for a fronto-parietal distinction related to the WM functions of processing and storing of information comes also from research employing neuroelectric brain imaging methods (Klimesch, 1999, 2012; Klimesch, Freunberger, Sauseng, & Gruber, 2008; Sauseng et al., 2010). These studies showed that theta oscillations relate to working memory processes and that theta synchronizes during WM processes as well as acts as a gating mechanism, providing optimal neural conditions for specific processing (Sauseng et al., 2010).

An alternative perspective has suggested that the dorsolateral region of the prefrontal cortex (DLPFC) supports storage as well as processing of WM functions (Courtney, 2004; Leung, Seelig, & Gore, 2004; Pessoa, Gutierrez, Bandettini, & Ungerleider, 2002) and that short term storage and manipulation of information actually activate the same brain areas (Veltman, Rombouts, & Dolan, 2003). Several neuroimaging studies (Narayanan et al., 2005; Veltman et al., 2003; Zarahn, Rakitin, Abela, Flynn, & Stern, 2005) have supported this viewpoint. To date, it seems that neuroimaging studies cannot clarify the conflicting perspectives on the role of the frontal and parietal brain areas in WM function.

The recent rediscovered noninvasive brain stimulation techniques for inducing reversible changes in brain activity have become a valuable tool to investigate the underlying mechanisms of human cognition (Kuo & Nitsche, 2012). Thus far, three main forms of low-intensity transcranial electrical stimulation have been used (for review, see Kuo & Nitsche, 2012; Utz, Dimova, Oppenländer, & Kerkhoff, 2010; Zaghi, Acar, Hultgren, Boggio, & Fregni, 2009): transcranial direct current stimulation (tDCS; a method in which low-intensity constant current is applied to the head), transcranial alternating current stimulation (tACS in which low-intensity alternating current is applied to the head), and transcranial random noise stimulation (tRNS in which electrical stimulation is

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applied within a broad frequency spectrum (0.1–640 Hz) with random noise distribution).

Most of the transcranial stimulation studies investigating the effects on WM performance stimulated the left DLPFC (Boggio et al., 2006, 2008; Fregni et al., 2005; Mulquiney, Hoy, Daskalakis, & Fitzgerald, 2011; Utz et al., 2010; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011). Stimulation increased WM performance on different storage-and-processing tasks (e.g., *n*-back speed of performance and accuracy; accuracy in a visual recognition and in a sequential-letter working memory task). In contrast, tRNS did not influence WM performance on an *n*-back task (Mulquiney et al., 2011). To our knowledge just one study (Fregni, Boggio, Nitsche, Rigonatti, & Pascual-Leone, 2006) investigated the influence of tDCS of the left DLPFC on WM storage capacity (digit span forward and backward), showing a significant increase in digit-span after tDCS. However, a generalization of this finding with regard to the relationship between the left DLPFC and WM storage capacity is difficult for two reasons. First, respondents who participated in the study were patients with depression, and second, the individuals were not exposed to verum and sham conditions.

Much less research has been conducted into stimulating parietal brain areas. Jacobson, Ezra, Berger, and Lavidor (2012) used anodal tDCS over the left intraparietal sulcus which had a positive effect on a verbal recognition memory task. In a second study Polanía, Nitsche, Korman, Batsikadze, and Paulus (2012) could show that left frontoparietal coupling in the theta band (0^0 phase tACS) increased speed of performance on a delayed letter discrimination task as compared to a sham condition. In a repetitive transcranial magnetic stimulation (rTMS) study it was shown that disruptive rTMS had a more pronounced influence on WM storage capacity when applied to parietal areas than when applied to DLPFC (Postle et al., 2006).

The aim of the present study is to further explore the relationship between working memory functions (e.g., storage capacity and executive processes like: inhibition of irrelevant items, monitoring of ongoing performance and updating representations in memory) and brain activity in frontal and parietal areas. For that purpose we analyzed the influence theta tACS (delivered to left/right parietal and left frontal brain areas) has on the performance of various tasks of WM storage capacity and executive processes. The nature of the study was exploratory. Our general hypothesis was that transcranial alternating current stimulation of different brain areas would be reflected in respondents' performance of WM tasks.

2. Method

2.1. Subjects

The sample included 36 right-handed individuals (27 females; average age = 20 years and 5 months; SD = 4.25 months), recruited from a group of students participating in a large scale resting eyes closed EEG study. They were divided into three groups—left frontal, left parietal and right parietal—receiving tACS with target electrodes placed over left frontal, left parietal or right parietal sites (see Fig. 1). The respondents of the three groups were equalized with respect to sex and performance on Wechsler (1981), digit span task administered prior to the experiment (left parietal group: $M = 7.00$; $SD = 1.00$; right parietal group: $M = 6.88$; $SD = 0.93$; left frontal group: $M = 6.96$; $SD = 1.32$). The respondents had a similar educational background, taking no medication and reporting no medical treatments or health problems. The experiment was undertaken with the understanding and written consent of each subject, following the recommendations of the ethics committee of the Slovene Psychological Association.

2.2. Design

The study was a single blind sham controlled experiment. Dependent variables were the aggregated outcome measures from the different memory tasks used and were based on Baddeley's (Baddeley et al., 2011) multi-component WM model which represents a broad theoretical framework allowing for experimental testing. The analysis of data was hierarchical. Starting by testing the influence of the three tACS protocols on storage and executive processes represented in the multi-component model as the episodic buffer and central executive. In the second step we separately analyzed the storage and executive control functions: (1) the influence of tACS protocols on spatial/verbal, and forward/backward storage capacity, and (2) the influence of tACS protocols on executive control.

2.3. Tasks and procedure

Respondents participated in 2 sessions—a sham and a verum tACS setting which were counterbalanced. The sham and verum settings were separated by 28 days. This time delay was needed to ensure that females on sham and verum settings were tested on the same day of their menstrual cycle. It was shown that the relative release of sexual hormones in different phases of the menstrual cycle affected cognitive responses of females (e.g., Amin, Epperson, Constable, & Canli, 2006; Berman et al., 1997). The duration of the menstrual cycle was determined with a questionnaire administered after the first tACS session. Most of the female participants had a regular 28 day menstrual cycle ($M = 28.42$ days; $SD = 0.73$ days).

In each setting respondents were exposed to sham/verum tACS for 15 min, then answered a questionnaire about their sensations during stimulation, after which they solved the WM tasks. The order of task presentation was rotated between respondents, but was the same for each subject in the sham and verum setting. All tasks were presented

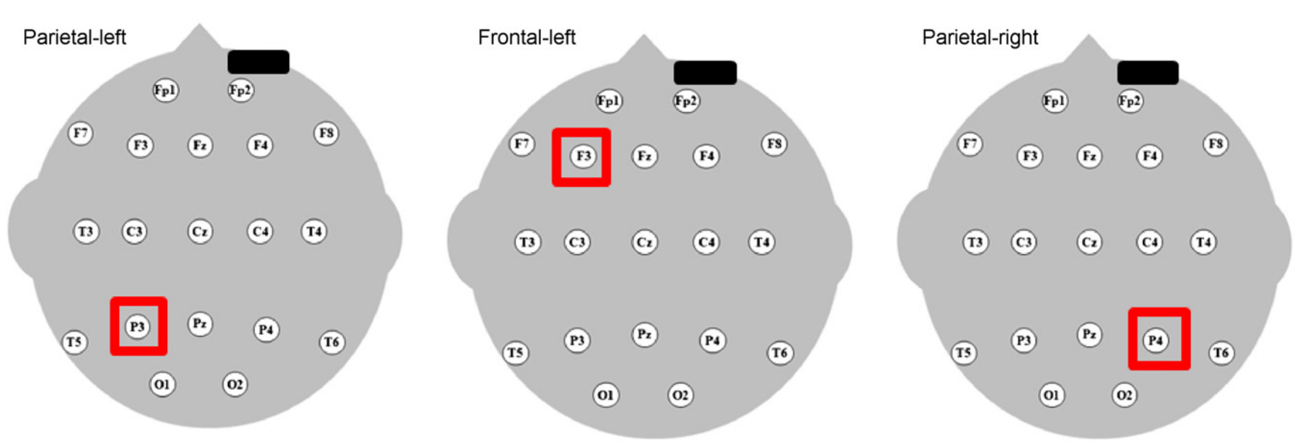

Fig. 1. Position of target electrodes (square) and return electrode (rectangle) for the three tACS protocols.