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Research report

Individual differences and specificity of prefrontal gamma frequency-tACS on fluid intelligence capabilities

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ABSTRACT

Emerging evidence suggests that transcranial alternating current stimulation (tACS) is an effective, frequency-specific modulator of endogenous brain oscillations, with the potential to alter cognitive performance. Here, we show that reduction in response latencies to solve complex logic problem indexing fluid intelligence is obtained through 40 Hz-tACS (gamma band) applied to the prefrontal cortex. This improvement in human performance depends on individual ability, with slower performers at baseline receiving greater benefits. The effect could have not being explained by regression to the mean, and showed task and frequency specificity: it was not observed for trials not involving logical reasoning, as well as with the application of low frequency 5 Hz-tACS (theta band) or non-periodic high frequency random noise stimulation (101–640 Hz). Moreover, performance in a spatial working memory task was not affected by brain stimulation, excluding possible effects on fluid intelligence enhancement through an increase in memory performance. We suggest that such high-level cognitive functions are dissociable by frequency-specific neuromodulatory effects, possibly related to entrainment of specific brain rhythms. We conclude that individual differences in cognitive abilities, due to acquired or developmental origins, could be reduced during frequency-specific tACS, a finding that should be taken into account for future individual cognitive rehabilitation studies.

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1. Introduction

High level cognitive processes such as consolidation of episodic memory traces (Marshall, Helgadottir, Molle, & Born, 2006), working memory (WM) (Polania, Nitsche, Korman, Batsikadze, & Paulus 2012), decision making (Sela, Kilim, & Lavidor, 2012) and logical reasoning (Santarnecchi, Polizzotto, et al., 2013) may benefit from noninvasive transcranial alternating current stimulation (tACS), particularly when the applied frequency coincides with the endogenous regional synchronization that accompanies the function of interest. These findings confirm experimental evidence indicating that tACS induces a reinforcement of ongoing brain oscillations by "entrainment" (Frohlich & Mccormick, 2010; Reato, Rahman, Bikson, & Parra 2010) or "resonance" phenomena of large-scale networks (Ali, Sellers, & Frohlich 2013; Antal & Paulus, 2013), an effect that might be exploited for rehabilitative or enhancement interventions with transcranial Electrical Stimulation (tES) in humans (Santarnecchi et al. 2015).

Whether tACS-induced cognitive enhancement takes place irrespective of pre-stimulation individual differences in performance (and-or underlying neurophysiological dynamics), or alternatively, depends on the individual's cognitive and-or oscillatory patterns profile, is still unknown. However, the latter scenario might better align with the documented state-dependency of tACS effect on the motor and visual systems, which suggests how the response to tACS is modulated by behavioral demands and consequently by the neurophysiological changes accompanied by these (Feurra et al., 2013; Kanai, Chaieb, Antal, Walsh, & Paulus, 2008). If this were the case, the dependency on individual cognitive -as well as purely neurophysiological- profile might represent a key feature in determining the potentials (and limits) for neuroenhancement applications.

In a previous study (Santarnecchi, Polizzotto, et al., 2013), 40 Hz-tACS (gamma-band) has been applied to the prefrontal cortex during a fluid intelligence (G*f*) task, which includes logical reasoning problems and relational problems. Briefly, logical reasoning refers to the ability to solve problems based on logical conditional arguments (e.g., where specific rule of inference "Modus Tollens" is applied: *if P then Q*; *not-Q*; e.g., "if there is a circle then there is a triangle. There is not a triangle. Therefore, there is not a circle"; see Fig. 1A- Logic), which have been demonstrated to mostly activate prefrontal structures (Prado, Van Der Henst, & Noveck, 2010). On the other hand, relational problems are based on perceptual relations (i.e., linear arguments as those in relational syllogisms, e.g., *P is to the left of Q; Q is to the left of R*; "The circle is to the left of the triangle. The triangle is to the left of the square. Therefore, the circle is to the left of the square"; see Fig. 1A-Relational) and require less prefrontal engagement in favor of higher parietal activation (Prado et al., 2010). By comparing 40 Hz tACS with other stimulation frequencies (5 Hz, 10 Hz, 20 Hz) and a sham condition, Santarnecchi, Polizzotto, et al. (2013) found a trial type-specific decrease in the time required to solve complex logical reasoning problems in healthy subjects. However, it is still unclear whether improvements in logical reasoning may occur as (1) a consequence of the modulation of brain dynamics leading to a change of cortico-spinal excitability —instead of a specific modulation of the brain rhythm(s) being targeted— or (2) as an indirect enhancement of other cognitive functions, such as WM, which is an integral part of G*f* abilities (Diamond, 2013). Moreover, given the positive correlation between G*f* and performance on a wide range of cognitive tasks, as well as its role as a predictor of both educational and professional success (Baltes, Staudinger, & Lindenberger, 1999; Gottfried, Fleming, & Gottfried 1998), understanding the role of individual cognitive differences in the response to tACS represents an important question for future application as well.

We tested these hypotheses in two experiments by applying different stimulation parameters, and during performance on a visuospatial WM task and a visuospatial abstract reasoning task commonly used for indexing G*f*.

2. Materials and methods

2.1. *Participants*

Participants were healthy right-handed individuals recruited from the University of Oxford vicinity. Fifty-eight subjects were included, after being screened for overt contraindications for tES, including personal and family history of epilepsy, unstable medical conditions, psychoactive or central nervous system-active medication, and recent migraine attacks. Twenty-four individuals (11 female) (23.8 ± 3.14 years) took part in Experiment 1, thirty-four individuals (17 female) (24.3 ± 2.76 years) took part in Experiment 2 [Gender, $\chi^2 = .98$, $p > .75$; Age, $t_{(56)} = -.88$, $p > .61$]. All participants provided written informed consent. Participants were compensated with £30 for their time. The study was approved by the Berkshire Ethics Committee (10/H0505/72).

2.2. *Experimental paradigm*

The aim of Experiment 1 was twofold: (i) testing for the effect of different tACS frequency on G*f* performance, as well as (ii) the potential concurrent effect of tACS on WM performance (see Fig. 1). Twenty-four participants performed G*f* and WM tasks (see the following paragraphs for a detailed description) while receiving 40 Hz (γ-band), 5 Hz (θ-band) or sham-tACS in a fully counterbalanced design (both task and stimulation order). In Experiment 2 ($n = 34$), we used the same experimental design, but replaced stimulation in θ-band with high-frequency transcranial random white noise (101–640 Hz) stimulation (tRNS). This allowed us to examine the role of frequency-specific resonance phenomena and potential modulation of cortical excitability as the mechanism of action for tACS-induced G*f* improvement, since tRNS is assumed to alter brain dynamics in a way that cortical excitability is modified (see below). Moreover, it also allowed replicating the findings from Experiment 1 in respect to individual differences as well as the role of WM.

High-frequency tRNS is a recently developed form of tES based on a random (i.e., not sinusoidal) electrical oscillatory spectrum (101–640 Hz), capable of inducing long-lasting effects on cortical excitability when applied on the scalp