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Research report

From amusic to musical?—Improving pitch memory in congenital amusia with transcranial alternating current stimulation

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HIGHLIGHTS

- Congenital amusia is associated with pitch perception and memory deficits.
- 35 or 90 Hz tACS was applied while amusics completed a pitch and visual memory task.
- 35 Hz tACS over the right DLPFC facilitated pitch memory in amusics selectively.
- 35 Hz tACS improved amusics' pitch memory to the level of healthy controls.
- The dysfunction of the DLPFC is causally related to pitch memory deficits in amusia.

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ABSTRACT

Brain imaging studies highlighted structural differences in congenital amusia, a life-long perceptual disorder that is associated with pitch perception and pitch memory deficits. A functional anomaly characterized by decreased low gamma oscillations (30–40 Hz range) in the right dorsolateral prefrontal cortex (DLPFC) during pitch memory has been revealed recently. Thus, the present study investigates whether applying transcranial alternating current stimulation (tACS) at 35 Hz to the right DLPFC would improve pitch memory. Nine amusics took part in two tACS sessions (either 35 Hz or 90 Hz) and completed a pitch and visual memory task before and during stimulation. 35 Hz stimulation facilitated pitch memory significantly. No modulation effects were found with 90 Hz stimulation or on the visual task. While amusics showed a selective impairment of pitch memory before stimulation, the performance during 35 Hz stimulation was not significantly different to healthy controls anymore. Taken together, the study shows that modulating the right DLPFC with 35 Hz tACS in congenital amusia selectively improves pitch memory performance supporting the hypothesis that decreased gamma oscillations within the DLPFC are causally involved in disturbed pitch memory and highlight the potential use of tACS to interact with cognitive processes.

1. Introduction

Music is an important trait of human culture. In order to process and understand music, it is essential to be able to perceive and memorize musical material such as musical pitches. However about four per cent of the population lack these abilities and have a congenital perception disorder, known as tone-deafness or congenital amusia [1,2], which is not caused by insufficient exposure to music, a hearing deficiency or intellectual impairment [3]. Behavioural research has shown that amusia is linked to pitch perception deficits [4,5]) and impaired pitch memory [6–10] whereas the visuo-spatial domain and processing of space are not affected (Tillmann et al. [11,12]). Recent studies have also indicated deficits in language perception or more specifically intonation perception (Patel et al. [13–15]).

Brain imaging studies have revealed structural and functional brain differences compared to healthy controls, predominantly in the frontal and temporal lobes [16–19,10]. Using voxel-based morphometry, Hyde et al. (2006) reported reduced white matter concentration in the right inferior frontal lobe in amusic individ-

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uals compared to controls, which was accompanied by more grey matter volume in the same region [15]. In addition, cortical malformations (e.g. thicker cortices) in the right inferior frontal gyrus and right auditory cortex in participants with congenital amusia compared to controls were found [17]. A functional magnetic resonance imaging (fMRI) study revealed abnormal deactivation of the right inferior frontal gyrus and reduced connectivity of this area to the auditory cortex in amusic brains [18]. Further support for a reduced fronto-temporal connectivity in congenital amusia was revealed by Loui et al. (2009) suggesting reduced fiber activity in the right arcuate fasciculus compared to matched controls [19]. Regarding the lateralization of the structural differences of amusics to healthy controls, a study by Mandell et al. (2007) also found a left fronto-temporal network being related to the Montreal Battery of Evaluation of Amusia (MBEA) scores in amusics [20]. A recent study by Albouy et al. (2013) investigated short-term memory for six-tone sequences in congenital amusics using magnetoencephalography (MEG) and voxel-based morphometry [10]. The study confirmed anomalies of grey and white matter concentrations in the right inferior frontal gyrus. Additionally, the study showed that during the retention of the pitch material the induced low gamma oscillations (30–40 Hz range) in the right dorsolateral prefrontal cortex (DLPFC) were lower in congenital amusics compared to healthy controls. This result suggests that the impairment in maintaining the pitch information in individuals with congenital amusia might be related to alterations of oscillatory activity in the low gamma range.

Non-invasive brain stimulation such as transcranial magnetic stimulation (TMS), transcranial direct and transcranial alternating stimulation (tDCS, tACS) allows to draw causal involvements of certain brain areas and their function on cognitive performances (e.g. [21] for a review) and have also been used for therapeutic interventions (e.g. [22] for a recent review). TACS is suggested to interfere with ongoing brain oscillations although the exact mechanisms behind the technique are not fully understood yet [23]. An alternating current with a specific frequency is applied and the endogenous ongoing brain oscillations may interact with the inserted exogenous oscillations and endogenous oscillations can synchronise with and be entrained by the stimulation frequency [24,25]. When stimulation is applied for a longer time period, tACS influences cortical excitability and can lead to neuroplastic reorganisation [24]. Previous studies have also shown the potential use to modulate perception and cognitive performances ([26] for a review). Helfrich et al. (2013) showed that 10 Hz tACS applied to the parieto-occipital cortex led to an improved performance in a visual target detection task which was traced back to an entrainment of alpha oscillations in the targeted area measured by electroencephalography (EEG) [27]. Laczo et al. (2012) applied tACS at different frequencies within the gamma range (40, 60 and 80 Hz) over the primary visual cortex and revealed that only 60 Hz tACS facilitated contrast perception [28]. Furthermore, working memory improved when performance was tested during online theta tACS over bilateral DLPFC compared to post-stimulation testing [29]. In this study, participants completed a 2-back word recognition task online to stimulation and a 2-back recall task after stimulation. Theta tACS facilitated online working memory performance significantly [29].

Gamma oscillations have been associated with memory functions in several domains [30–32]). In the auditory domain, for example, increased gamma oscillations have been found in inferior frontal and temporal areas during pattern working memory of syllables [31]. Furthermore, a review by Jensen et al. (2007) points out the connection of gamma oscillations and the representation of task-relevant information in attention and memory processes [33].

The aim of the present study was to investigate whether applying gamma oscillations at 35 Hz to the right DLPFC using tACS can facilitate pitch memory abilities in congenital amusia. Building on the results by Albouy et al. (2013) [10], who showed decreased low gamma oscillations (30–40 Hz) in the right DLPFC while amusics perform a pitch memory task, we hypothesized that (i) amusics exhibit a selective impairment in pitch memory compared to controls before stimulation and (ii) that tACS applied with a frequency of 35 Hz to the right DLPFC will improve pitch memory performance in amusics to the level of healthy controls.

2. Material and methods

2.1. Participants

Nine amusics (7 female; age: 24.89 ± 1.33 years (mean ± standard error of the mean, SEM); musical education: 3.22 ± 1.18 years) and eight matched control participants (7 female; age: 23.75 ± 0.70 years; musical education: 3.00 ± 1.25 years) took part in the present study. This modest sample size is common for studies including participants with congenital amusia. One amusic was excluded from the data analysis as she performed more than three standard deviations above the mean in the pitch memory task. All participants were native speakers of German, right-handed, as confirmed by the Edinburgh Handedness Inventory [34], and had normal hearing (defined as a mean hearing level of 20 dB or less in both ears), which was assessed by pure tone audiometry at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz. In addition, exclusion criteria were history or family history of epileptic seizures or any other neurological or psychiatric disorder, metallic implants and drug or alcohol abuse. To be considered as amusic, participants had to score below a cut-off score of 75% on the first four subtests of the MBEA [2]; see material for further details) while all controls scored 88% or higher on the same four subtests. The mean score of the amusic group was 20.26 ± 1.52 for the pitch-based subtests and 24.12 ± 2.86 for rhythm (maximum score 30). The results of the control group (pitch-based mean: 27.33 ± 1.36, rhythm mean: 27.06 ± 1.18) differed significantly from the values of the amusic group [$t(16) = 9.79$, $p < .001$ for pitch-based and $t(16) = 2.68$, $p = .018$ for rhythm].

The study was approved by the ethics committee of the Medical Department of the Heinrich-Heine-University in Düsseldorf. Prior to the study all participants gave their informed written consent to take part and received a small monetary reimbursement for their participation.

2.2. Material

The **Montreal Battery of Evaluation of Amusia** (MBEA) [2] was used to categorize the participants as amusic and normal controls. The MBEA contains six subtests that assess several components of musical perception and memory and is the most widely used tool to diagnose congenital amusia [6,10,16]. The first three subtests evaluate melodic organization or pitch perception (scale, contour and interval), the fourth and fifth subtests evaluate temporal organisation (rhythm and metre) and the remaining sixth test is a memory test. Each subtest consists of 30 trials. For scoring, the correct answers on each subtest are summed up. As the cut-off score was set to 75%, participants had to score below 23 correct answers to be considered amusic [2]. The amusic participants completed the MBEA for a firm diagnosis twice, once online and once in the laboratory, to ensure that participants were categorized as amusics correctly. In addition, all participants answered a detailed questionnaire about their musical and linguistic background, ensuring that all participants were native speakers of German and that they had no knowledge of Sanskrit, Hindi or any other language written