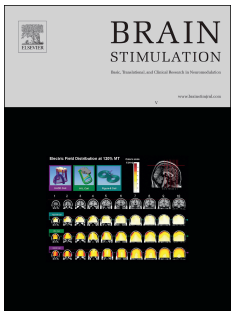

A person with frontotemporal dementia shows increased metabolic rate across multiple brain regions after a series of tDCS sessions

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A person with frontotemporal dementia shows increased metabolic rate across multiple brain regions after a series of tDCS sessions

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Dear Sir,

In a previous study [1], we explored the effects of transcranial direct current stimulation (tDCS) on reducing response times in an untrained N-Back task [2]. Our findings indicated that the active tDCS conditions resulted in greater reductions in response times compared to the SHAM condition, with the left-hemisphere targeting montage appearing to be the most effective. These results prompted us to investigate whether this tDCS protocol could elicit measurable neurological changes in the brain. To accomplish this, we preselected a male participant who had previously exhibited tDCS effects to complete two rounds of N-Back practice, one with SHAM and another with tDCS, which included pre- and post-tDCS FDG-PET scans to examine possible glucose uptake changes. This participant was diagnosed with behaviour variant frontotemporal dementia (FTD) at 58 due to symptoms such as aggression, disorganization, and apathy, although his cognitive impairment remains mild. In both 2017 and 2021, he participated in tDCS studies [1,3], demonstrating greater improvements in the active tDCS conditions compared to the SHAM conditions and displaying improved behaviour at home (see testimonial video). As detailed below, our analysis revealed higher glucose metabolism levels in the post-tDCS FDG-PET scans of our participant. Although these findings reflect a single participant, we argue they are significant for two reasons. First, to date, only eight tDCS PET studies have been conducted [4], and this case report provides valuable new insights into the limited literature on the topic. Second, a previous tDCS study revealed that tDCS may preserve metabolic rates in the left middle/inferior temporal gyrus of individuals with Alzheimer's Disease (AD), a critical area impacted by the disease [5]. However, FTD participants, who also experience metabolic changes, were not included in that study. Thus, we believe this case report is the first FDG-PET study involving a participant with FTD.

Methods

Study Design

The study involved the participant completing two rounds of nine N-Back practice sessions each, spanning over three weeks. During each session, the participant practiced the N-Back for 20 minutes and simultaneously received either SHAM or active tDCS, depending on the round. The first week included a baseline evaluation on Tuesday and practice sessions on Thursday and Friday. The second week involved practice sessions on each weekday, while the third week included practice sessions on Monday and Tuesday, followed by a second evaluation on Wednesday, with a concurrent 20 minutes of SHAM or active tDCS, depending on the round. Two weeks after the second evaluation, the participant underwent the same evaluation without SHAM or active tDCS. The first round involved SHAM, while the second round involved active tDCS to control for the effects of novelty. The second round of training commenced after a 2-month break to eliminate the possibility of any practice effects. Stimulation condition order was concealed from the participant.

tDCS Methods

We aimed to investigate whether the montage previously demonstrated to be effective [1] could produce discernible changes in glucose uptake in our participant. Therefore, we maintained all the components of the montage used. Specifically, we placed the anode (5 x 7 cm) over the right supraorbital region and the cathode (5 x 7 cm) posteriorly over the occiput, at an intensity of 4 mA, which the participant tolerated.

Imaging Methods

The study involved pre- and post-stimulation scans, with the former being conducted in the week prior to practice sessions, and the latter taking place after the second evaluation session on Wednesday of the third week. Both FDG-PET and structural MRI scans were conducted to enable the quantification of metabolic changes in various regions of the brain. Metabolism values for different brain areas were calculated using a quantitative glucose metabolism ratio based on the cerebellum as a reference (SUVR). Larger scores indicate higher metabolic rates. The use of the cerebellum as a reference is a common practice when studying people with dementia, as it is believed to be the least affected by amyloid in individuals with AD, and for this reason has been extended to other populations, such as elderly individuals or people with FTD.

Results

In our previous study, we found that the largest effects were observed during the two-week post-stimulation evaluation. Therefore, we decided to compare the N-Back response times at baseline with those obtained two weeks after stimulation. In the active tDCS condition, response times showed a 14% improvement (from 12,591 ms to 10,776 ms) versus an 8% improvement (from 10,754 ms to 9,851 ms) when the task was practiced with SHAM stimulation. We subsequently examined the ratio values in the left frontal region, where the anode electrode was located, and found that the ratio values increased by approximately 23%, from an average of 1.04 to 1.27. However, as our montage was designed to stimulate the entire left hemisphere, we expanded this examination to other regions and found higher ratio values was true for most brain regions, including those in the right hemisphere (see supplementary data). For instance, the ratio increased from 0.81 to 0.93 and from 0.85 to 1.02 in the left and right temporal poles, respectively. Figure 1 shows the percentage increase across different regions.

Discussion

N-Back response times decreased more when practice sessions were accompanied with active tDCS, and post FDG-PET scans found higher metabolic rates in multiple regions. However, being a case report of one participant, the study is anecdotal, uncontrolled, and possibly influenced by factors other than the intervention. Using the cerebellum as a referent (SUVR) may also be problematic, as active tDCS could specifically affect this area, leading to higher denominator values and lower ratio values across different regions; in turn reducing the chance of observing changes while increasing Type 2 error. However, in this study, significant increases were observed in multiple areas and suggests a non-focal impact of the stimulation, consistent with a montage designed to stimulate the entire left hemisphere. Thus, the results seem reliable because the cerebellum was not uniquely impacted by tDCS. Overall, these findings suggest that tDCS may have potential as a therapeutic intervention for FTD, but further research is needed to establish its efficacy.

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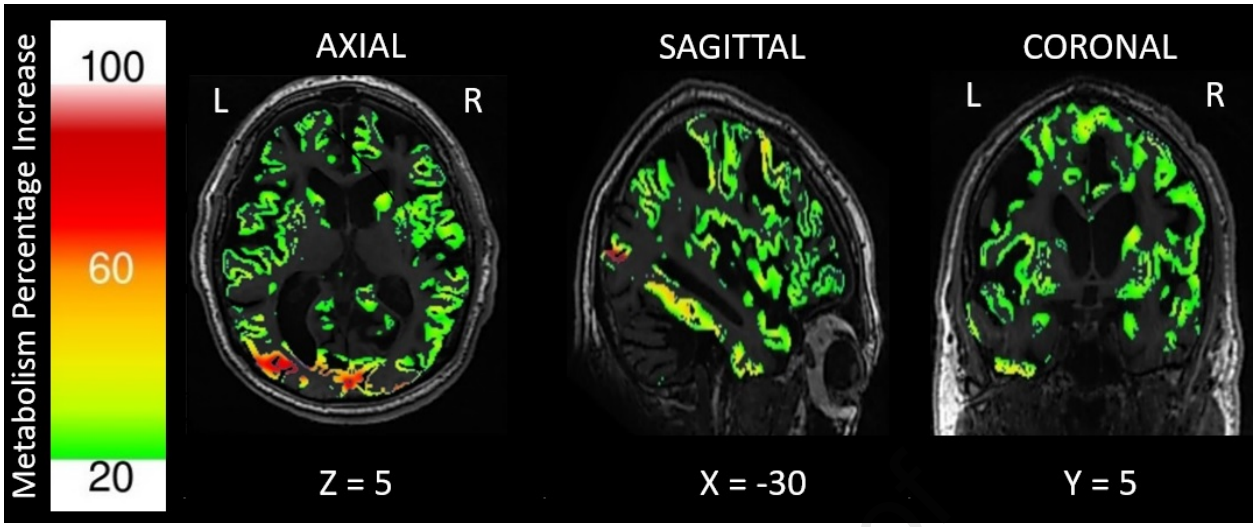

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: