



## High intensity aerobic exercise does not prime the brain for anodal transcranial direct current stimulation



### Keywords:

Cognition  
Working memory  
High intensity interval training  
Brain derived neurotrophic factor  
Transcranial magnetic stimulation  
Functional near-infrared spectroscopy

### Dear Editor,

The benefits of both regular and acute exercise on cognitive function are well-established. One candidate mechanism is the increase in brain derived neurotrophic factor (BDNF), which is involved in exercise-induced neuroplasticity [1]. An increase in serum BDNF after a single exercise session may create favourable conditions for adaptive plasticity [2], and has also been shown to influence anodal transcranial direct current stimulation (a-tDCS) in mice [3]. We investigated the acute effects of a single bout of high-intensity interval training (HIIT) performed prior to dorsolateral pre-frontal cortex (DLPFC) a-tDCS on cognitive performance, serum BDNF, and the cerebral haemodynamic response in healthy adults. We hypothesised that exercise would increase serum BDNF and the cerebral haemodynamic response in the DLPFC, augmenting the effects of a-tDCS.

In a randomised cross-over study design, 24 sedentary but otherwise healthy participants ( $22.2 \pm 2.9$  years, 12 female) performed three double-blind testing sessions: 1) *Rest + tDCS*, seated rest followed by a-tDCS, 2) *Ex + sham*, exercise followed by sham-tDCS, and 3) *Ex + tDCS*, exercise followed by a-tDCS. Two-way repeated measures ANOVA was used to determine the effect of within-subject factors CONDITION (*Rest + tDCS*, *Ex + sham*, *Ex + tDCS*) and TIME (*pre*, *post*).

Exercise involved 20min of high intensity interval training (HIIT) on a stationary bicycle, with a total of  $5 \times 2$ min work periods completed at a pace of 100 revolutions per minute and 80% maximal heart rate (HR), separated by 2min active recovery. Rating of perceived exertion and HR were recorded at the end of each work period to ensure their consistency across the *Ex + sham* and *Ex + tDCS* sessions (all  $p > .05$ ).

Anodal tDCS was applied using a Starstim DC stimulator (Neuro-electrics, Barcelona) for 20min, immediately following exercise, while seated and resting [4]. Current (1mA) was delivered through  $25\text{cm}^2$  saline-soaked sponge electrodes (current density  $0.04\text{mA}/\text{cm}^2$ ). The anode was placed on the F3 site, and the cathode placed over the contralateral supraorbital region. Sham-tDCS involved a 15sec current ramp-up/down.

Cognition was assessed using a computerised battery performed in a random block design. Tasks included single and two-choice reaction time, congruent and incongruent Stroop, and 2-/3-back working memory. There were main effects for time in the single-choice reaction time ( $F_{(1, 22)} = 8.59, p = .008$ ) and the incongruent Stroop tasks ( $F_{(1, 22)} = 4.66, p = .042$ ), with a mean increase in response time and performance across all conditions of 9.6 ms (Fig. 1a) and 5.6% respectively (composite score for response time and accuracy) (Fig. 1b). No interaction and no main effect for condition were found for either task. No significant main effects or interactions were observed for other tasks.

During the 2-/3-back tasks, a single-channel functional near-infrared spectroscopy (fNIRS) device (Portalite, Artinis Medical Systems, The Netherlands) was used to record haemodynamic response, as measured by a change in oxyhemoglobin (HbO) level over the left DLPFC (F3 site). There was no interaction ( $F_{(2, 44)} = 2.05, p = .141$ ) and no main effect for condition ( $F_{(2, 44)} = 1.85, p = .170$ ). A significant main effect for time was detected ( $F_{(1, 22)} = 13.87, p = .001$ ). There were increases in HbO following all conditions: *Rest + tDCS* (25.5%), *Ex + sham* (52.1%), and *Ex + tDCS* (63.4%).

A blood sample was drawn from the median cubital vein in a subgroup of 12 participants, centrifuged at 12,000g for 10min at  $4^\circ\text{C}$ . Plasma was frozen at  $-80^\circ\text{C}$  for later analysis. Multiplex immunoassay was performed by Crux Biolab (Melbourne, Australia) with a custom-designed Quantibody human-specific protein array (RayBiotech, USA) to detect BDNF concentration. No significant interactions or main effects were observed ( $p > .05$ ).

The increase in response time for the simple reaction time task may be due to a fatigue effect induced by the 2hr duration of the session. A lack of significant interaction indicates that neither exercise, a-tDCS nor the combined intervention were effective in attenuating performance declines across the session. The modest improvement in performance on the incongruent Stroop task

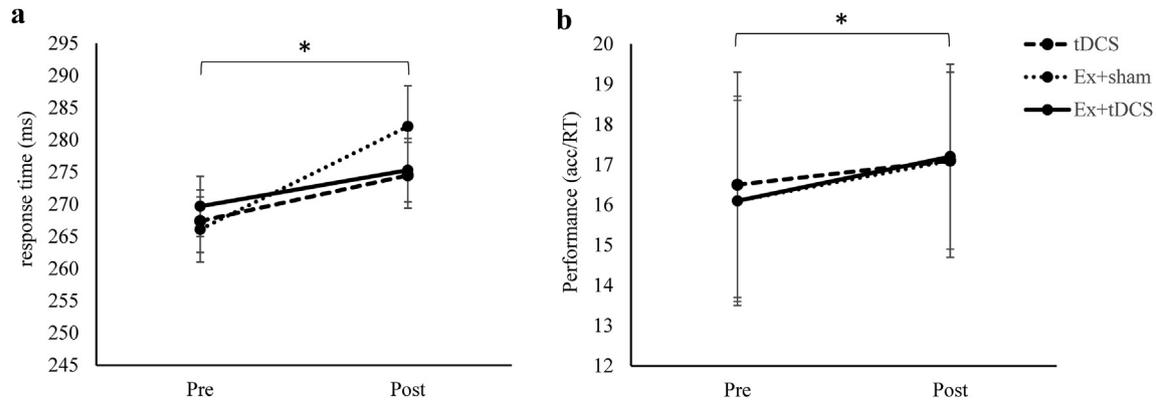


Fig. 1. Response time for simple reaction task (a), and composite performance score for incongruent Stroop task (b). \* denotes significant main effect for time.

may be attributed to practice on the task. Overall, the lack of significant differences in behavioural outcomes was contrary to our hypothesis, and contrasts previous literature investigating HIIT and a-tDCS in isolation. However, our findings are consistent with recent meta-analyses showing small effects that are highly variable [5,6]. Previous research has shown that delivery of tDCS while engaging the specific brain region during tDCS delivery may influence the outcomes of stimulation [7,8]. In this study, the delivery of a-tDCS during seated rest may have contributed to the null-finding.

The intensity of acute exercise has been reported as a key moderator in cognitive outcomes. The ‘inverted-U’ hypothesis proposes that moderate intensity exercise is optimal for enhancing arousal, while the ‘drive-theory’ suggests that intensity-dependent physiological responses to exercise promote larger improvements in high-order cognitive tasks [9]. As such, it would be reasonable to hypothesise greater improvements in the incongruent Stroop and n-back tasks, however our results failed to support this. More recently, the influence of exercise intensity on cognitive performance has been suggested to differ depending on the participant’s level of aerobic fitness [9], with highly active participants exhibiting greater post-exercise increases [10]. We recruited sedentary participants, which may have contributed to the non-significant changes in cognitive performance and levels of circulating BDNF.

In agreement with previous studies [9], fNIRS measures showed an increase in cerebral haemodynamic response following all conditions. The combination of a-tDCS and HIIT did not produce a cumulative effect. Our behavioural data (i.e., 2- and 3-back performance) associated with the fNIRS measures did not improve following any of the conditions, which may be due to fatigue.

In conclusion, this study showed that 20mins of HIIT exercise does not prime the brain for a-tDCS, producing no cumulative benefits on cognition, BDNF or cerebral haemodynamic response in an acute setting. Additionally, a-tDCS alone did not modulate cognitive performance in healthy adults. The neurophysiological effects of a single session of HIIT may be short-lasting, and are likely to be dependent on the fitness level of the individual.

### Declaration of interest statement

This work was supported by the Deakin University Faculty Research Development Scheme [00-26-2016].

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.brs.2019.04.007>.

### References

- [1] Szuhany KL, Bugatti M, Otto MW. A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *J Psychiatr Res* 2015;60:56–64. <https://doi.org/10.1016/j.jpsychires.2014.10.003>.
- [2] Huang T, Larsen KT, Ried-Larsen M, Moller NC, Andersen LB. The effects of physical activity and exercise on brain-derived neurotrophic factor in healthy humans: a review. *Scand J Med Sci Sports* 2014;24(1):1–10. <https://doi.org/10.1111/sms.12069>.
- [3] Meinzer M, Antonenko D, Lindenberg R, Hetzer S, Ulm L, Avirame K, et al. Electrical brain stimulation improves cognitive performance by modulating functional connectivity and task-specific activation. *J Neurosci* 2012;32(5):1859–66. <https://doi.org/10.1523/jneurosci.4812-11.2012>.
- [4] Hoy KE, Emonson MR, Arnold SL, Thomson RH, Daskalakis ZJ, Fitzgerald PB. Testing the limits: investigating the effect of tDCS dose on working memory enhancement in healthy controls. *Neuropsychologia* 2013;51(9):1777–84. <https://doi.org/10.1016/j.neuropsychologia.2013.05.018>.
- [5] Hill AT, Fitzgerald PB, Hoy KE. Effects of anodal transcranial direct current stimulation on working memory: a systematic review and meta-analysis of findings from healthy and neuropsychiatric populations. *Brain Stimul* 2016;9(2):197–208. <https://doi.org/10.1016/j.brs.2015.10.006>.
- [6] Batsikadze G, Moliadze V, Paulus W, Kuo M-F, Nitsche MA. Partially non-linear stimulation intensity dependent effects of direct current stimulation on motor cortex excitability in humans. *J Physiol* 2013;591(7):1987–2000. <https://doi.org/10.1113/jphysiol.2012.249730>.
- [7] Martin DM, Liu R, Alonzo A, Green M, Player MJ, Sachdev P, et al. Can transcranial direct current stimulation enhance outcomes from cognitive training? A randomized controlled trial in healthy participants. *Int J Neuropsychopharmacol* 2013;16(9):1927–36. <https://doi.org/10.1017/S1461145713000539>.
- [8] Silvanto J, Muggleton N, Walsh V. State-dependency in brain stimulation studies of perception and cognition. *Trends Cognit Sci* 2008;12(12):447–54. <https://doi.org/10.1016/j.tics.2008.09.004>.
- [9] Basso JC, Suzuki WA. The effects of acute exercise on mood, cognition, neurophysiology, and neurochemical pathways: a review. *Brain Plast* 2017;2(2):127–52. <https://doi.org/10.3233/BPL-160040>.

- [10] Zoladz JA, Pilc A, Majerczak J, Grandys M, Zapart-Bukowska J, Duda K. Endurance training increases plasma brain-derived neurotrophic factor concentration in young healthy men. *J Physiol Pharmacol* 2008;59(7):119–32.

Ashlee M. Hendy\*, Helen Macpherson, Nathan D. Nuzum, Paul

A. Della Gatta, Sarah E. Alexander

*Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Faculty of Health, Deakin University, Geelong, Victoria, Australia*

Kate E. Hoy

*Monash Alfred Psychiatry Research Centre, The Alfred and Monash University Central Clinical School, Victoria, Australia*

Peter G. Enticott

*Cognitive Neuroscience Unit, School of Psychology, Deakin University, Geelong, Victoria, Australia*

Wei-Peng Teo

*Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Faculty of Health, Deakin University, Geelong, Victoria, Australia*

\* Corresponding author. Institute for Physical Activity and Nutrition (IPAN) School of Exercise and Nutrition Sciences Faculty of Health, Deakin University 75 Pigdons Rd, Waurn Ponds, 3216, Victoria, Australia.

E-mail address: [a.hendy@deakin.edu.au](mailto:a.hendy@deakin.edu.au) (A.M. Hendy).

30 March 2019

Available online 16 April 2019