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Original Article

Elite Cyclists with Type 1 Diabetes Show Acceptable Glycemic Excursions During a Time-Trial Performance Under High-Definition Transcranial Direct Current Stimulation

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ABSTRACT

Objective: To evaluate the effects of bilateral dorsolateral prefrontal cortex high-definition transcranial direct current stimulation (HD-tDCS) on glycemic excursions during a time-trial performance in elite cyclists with type 1 diabetes (T1D).

Methods: In a double-blind, randomized crossover order, 9 elite cyclists with T1D (no complications) underwent either HD-tDCS (F3 and F4) or control (SHAM) and completed a constant-load trial at 75% of the second ventilatory threshold plus a 15-km cycling time trial.

Results: Real-time continuous glucose monitoring revealed similar glycemic variability between the 2 conditions, showing a significant effect of time but no interaction (stimulation × time) or stimulation effect.

Conclusion: Because glycemic control is crucial for both health and performance, these findings suggest that HD-tDCS could be safely used to enhance performance in athletes with T1D and potentially in a broader active T1D population.

Introduction

Patients with type 1 diabetes (T1D) mellitus are typically challenged by glycemic fluctuations during exercise. There is considerable variability in the glycemic responses to physical activity in real-world scenarios. This variability is influenced by factors such as the type of sport, individual characteristics (participant's fitness level), treatment strategies, and psychosocial factors. Typically, 30 minutes of aerobic exercise of moderate intensity causes a drop in blood glucose levels, whereas more intensive aerobic exercise/anaerobic exercise may cause hyperglycemia in the fasted state and a rise in lactate level.[1] Despite this, there is still limited understanding of how these variables may impact blood glucose responses. Enhancing this knowledge would significantly improve the effectiveness of the diabetes self-management. For instance, postexercise glucose stabilization is a critical concern for individuals with T1D, emphasizing the need for tight glycemic control for both general health and performance objectives.

We recently applied high-definition transcranial direct current stimulation (HD-tDCS)—a neuromodulation enhancer—in both healthy elite cyclists[2,3] and those with T1D[4] to improve endurance performance. Transcranial direct current stimulation (tDCS), a noninvasive neuromodulatory method, applies weak direct current to the scalp (usually 1-2 mA) through large pads, creating an electric field that modifies cortical excitability by generating excitatory or inhibitory responses.[5] It is widely used in neurologic rehabilitation, cognitive enhancement, and psychiatric treatment[6] (Fig. 1). Some research explored the impact of HD-tDCS on motor skill learning showing the enhancement of motor learning processes, which could have implications for sports training. Specific

Abbreviations: CGM, continuous glucose monitoring; CLT, constant-load trial; HD-tDCS, high-definition transcranial direct current stimulation; PFC, prefrontal cortex; T1D, type 1 diabetes; tDCS, transcranial direct current stimulation; TT, time trial.

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findings related to sports and exercise involved aspects such as endurance, strength, or reaction time. tDCS has been claimed to boost several indicators of physical fitness, from sprint and endurance cycling to jumping, pinch force production, and dynamic balance. However, a high individual variability was reported in the effects of tDCS. For instance, anodal tDCS yield inconclusive results on endurance performance,[7-10] attributed to electrode type and position. Traditional tDCS, using 2 large pads, has low focality and associated risks. HD-tDCS, a recent variant, enhances focality with an array of small circular electrodes (3-5 cm^2), minimizing unintended influences on nontargeted areas.[11] Our recent studies using HD-tDCS over the prefrontal cortex (PFC) have demonstrated improved endurance performance in both long and short time trials (TTs) without altering physiologic responses during isotime TTs (monitored at the same time points during a set distance, eg, 15 km) in elite road cyclists.[2,3] HD-tDCS may also reduce perceived effort during exercise by affecting sensory signals from PFC-connected areas.[12] Improved performance appeared to be linked to a higher power output—to—perceptual-measure ratio. This suggests that upregulating PFC could enhance endurance performance. Anodal tDCS has shown effects on glucose regulation and metabolic functioning in healthy individuals.[13] Our previous research extended these benefits to a glucose-challenged model, specifically T1D,[4] prevalent in high-level cycling[14] and swimming. We previously investigated the effects of HD-tDCS on high-level cyclists with T1D, monitoring both performance and glycemic responses after stimulation, a novel aspect in empirical verification.[4] Particularly in this study, we sought to evaluate the effects of bilateral dorsolateral PFC HD-tDCS on glycemic excursions during a TT performance in elite cyclists with T1D.

Highlights

- HD-tDCS is safe for elite cyclists living with T1D.
- T1D elite cyclists show acceptable glycemic fluctuations during trial under HD-tDCS.
- HD-tDCS could enhance performance in elite cyclists via PFC upregulation.
- HD-tDCS can be safely used as a performance enhancer in athletes with T1D.

Clinical Relevance

This double-blind, crossover study explores high-definition transcranial direct current stimulation (HD-tDCS) effects on glycemic excursions during a cycling time trial in elite cyclists with type 1 diabetes. Although HD-tDCS did not significantly affect glycemic variability, it safely improved endurance performance. These findings propose potential applications of HD-tDCS for enhancing performance in athletes and active diabetic people.

Methods

Experimental Design

In a double-blind, randomized crossover order, international-level road male cyclists (Table) with T1D and no complications underwent either HD-tDCS (F3 and F4) or control (SHAM) and completed a cycling constant-load trial (CLT) at 75% of the second ventilatory threshold plus a 15-km cycling TT.

In the HD-tDCS condition, the anodes were set to deliver a total current of 1.5 mA, and the return electrodes shared the same current intensity (0.5 mA each) for a duration of 20 minutes at a current density of 0.059 mA/cm^2. At the beginning and end of stimulation, there was a gradual 20-second increase and decrease in current intensity. In the SHAM condition, the electrode placement remained identical, but stimulation was active only during the 30-second onset and offset durations.

The experimental procedures concerning either the cycling performance (including the preparation) or the HD-tDCS (Neuroelectrics) followed those of a previous study.[4] Throughout the cycling performance, the blood glucose levels were read out by

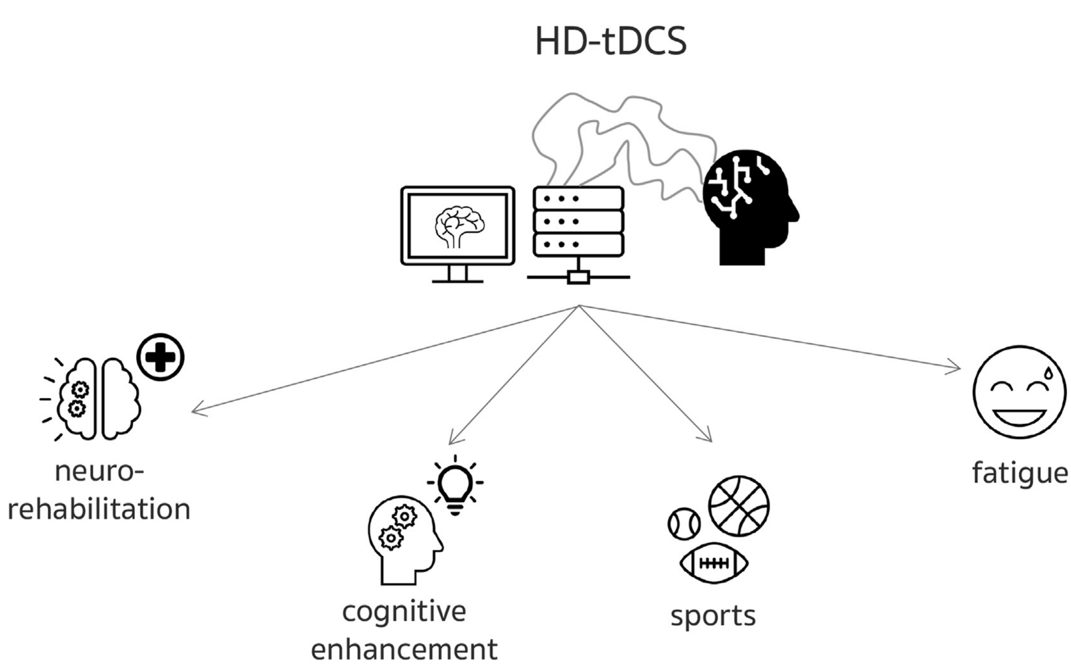

Fig. 1. Depiction summarizing the applications of high-definition transcranial direct current stimulation (HD-tDCS).

Table
Characteristics of the 9 International-Level Cyclists With Type 1 Diabetes Mellitus

Characteristic	Values
Age (y)	28 ± 3.5
BMI (kg/m^2)	20.8 ± 1.3
Diabetes duration (y)	>10
Insulin doses (minimum to maximum, IU/d)	23 ± 7 to 25 ± 10
VO_2 peak (mL/min/kg)	65.3 ± 1.7
Training frequency (d/wk)	>5

Abbreviations: BMI = body mass index; VO_2 peak = peak oxygen uptake.

continuous glucose monitoring (CGM) (G6; Dexcom) every 3 minutes. Every athlete received detailed information about the procedures and associated risks before providing written informed consent to partake in the study. The study design and procedures received approval from the local research ethics committee of the Università degli Studi di Milano (number 121/19, attachment 5) and adhered to the ethical principles outlined in the World Medical Association Declaration of Helsinki concerning medical research involving human participants. Participants were not engaged in the study's design, implementation, reporting, or dissemination plans.

Statistical Analysis

All data are presented as mean (SD). The assumptions of normality and sphericity were checked using the Shapiro-Wilk test and the Mauchly test, respectively. All data showed normal distribution, whereas the Greenhouse-Geisser correction was used when sphericity was not met. A 2-way (time and stimulation) repeated-measures analysis of variance was performed to analyze blood glucose concentrations by CGM during CLT and TT. The data analysis was performed using SPSS software (version 26.0; SPSS Inc).

Data and Resource Availability

The data sets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request. No applicable resources were generated or analyzed during the current study.

Results

Comparing the 2 conditions by real-time CGM readouts (Fig. 1), cyclists showed similar glycemic variability in any part of the experimental session, with a significant effect of time ($F = 26.32$; $P < .0001$), but no interaction (stimulation × time) ($F = 0.08$; $P > .99$) or effect of stimulation ($F = 0.077$; $P = .79$) (Fig. 2). Furthermore, CGM data were stable for the 3 days preceding and following the tests.

As elsewhere reported, no differences were registered in both conditions during CLT and TT regarding the physiologic parameters (lactate, glycemia, heart rate, and cadence).[4] Instead, after HD-tDCS,

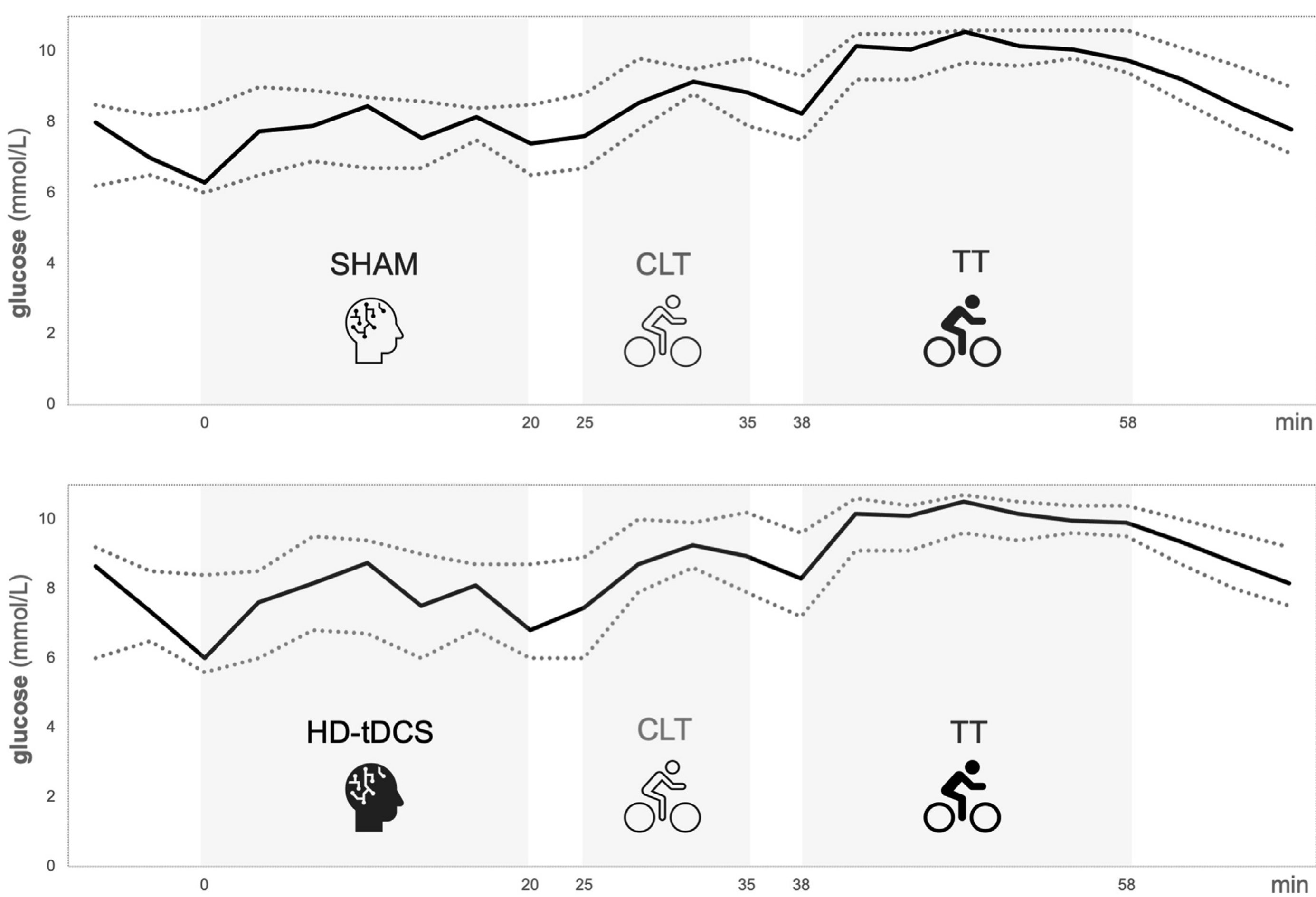

Fig. 2. Glycemic excursions in elite cyclists with type 1 diabetes during the experimental session under SHAM (top) or high-definition transcranial direct current stimulation (HD-tDCS) (bottom) conditions. Bold lines indicate mean values; dotted lines indicate minimum and maximum values. Continuous glucose monitoring readings were sampled every 3 minutes. *CLT* = constant-load trial; *TT* = time trial.

the total time to cover the TT was approximately 4% faster ($P < .01$) and was associated with higher mean power output ($P < .01$), rate of power/perception of effort ($P < .01$), and power/heart rate at isotime ($P < .05$) than those under the SHAM condition.

Discussion

Managing glucose during exercise becomes challenging due to the unpredictable glycemic responses in T1D. Elite athletes with this condition may face even more pronounced difficulties, potentially impacting sports performance. Previously, the main strategies and factors affecting the magnitude of glucose drop during exercise were (1) the noncompetitiveness of the activity, (2) low blood glucose level prior to exercise, and (3) elevated baseline glucose level.[1] Before the presented experimental setting, the use of a neuromodulator performance enhancer remained unexplored as to the real-time glycemic responses. Overall, these study findings provided no evidence of a difference in the glycemic excursions registered in the cyclists whether they underwent the HD-tDCS intervention or the SHAM. One possible explanation for this result resides in the intensity of the performance: although the TT is maximal, its duration was probably insufficiently prolonged for these high-level athletes to elicit a catecholamine-induced increase in the rate of glucose appearance through hepatic glycogenolysis.[15] Instead, after HD-tDCS, cyclists achieved performance in both the time to cover the TT distance and the associated power output. These gains, approximately 4%, are of critical relevance in competition because they could lead to overcoming opponents with <1% difference. It is also plausible that these cyclists did not perceive the experiment as stressful because they may perceive a competitive event (especially of a longer duration). It is indeed known that individual's self-perception of competition stress could affect glycemic variability.[1]

In conclusion, upregulation of PFC procured by HD-tDCS could enhance endurance performance in high-level cyclists with T1D, with acceptable glycemic excursions before, during, and after effort. Given that glycemic control becomes of paramount interest not only for health but also for performance goals, these findings suggest that HD-tDCS can be safely used as a performance improvement device in athletes with T1D and possibly in a wider population of active subjects with T1D. In fact, the capability to better understand blood glucose fluctuations during and after exercise represents a significant advancement not confined to the use of HD-tDCS: it broadens our understanding of physical activity safety as an essential part of a healthy lifestyle for individuals living with T1D, as well as for the general population.

Limitations

The primary limitation of this study is the relatively small sample size. This stems from the challenge of recruiting high-level athletes with T1D for multiday standardized laboratory research projects, given their demanding racing calendars and training schedules. Another limitation is the absence of monitoring brain responses during exercise and after stimulation using techniques such as electroencephalography or near-infrared spectroscopy. This limitation only allows for speculation regarding the physiologic mechanisms through which HD-tDCS may have enhanced performance.

Disclosure

The authors have no conflicts of interest to disclose.

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Author Contributions

R.C. and L.F. conceptualized the study; G.G. developed the methodology; R.C., G.G., A.M., and L.F. curated the data and performed investigation; G.G. and A.M. were responsible for the software process; R.C. and L.F. performed formal analysis; L.L. was responsible for the resources; R.C., A.M., and L.F. performed visualization; R.C. and L.F. supervised the study; L.F. was responsible for project administration; R.C. and L.F. wrote the original draft of the manuscript; L.L. reviewed and edited the manuscript. All authors reviewed and approved the final manuscript.

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