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Narrative Review

Analgesics and Sport Performance: Beyond the Pain-Modulating Effects

Darias Holgado, MD, James Hopker, PhD, Daniel Sanabria, PhD, Mikel Zabala, PhD

Abstract

Analgesics are used widely in sport to treat pain and inflammation associated with injury. However, there is growing evidence that some athletes might be taking these substances in an attempt to enhance performance. Although the pharmacologic action of analgesics and their use in treating pain with and without anti-inflammatory effect is well established, their effect on sport performance is debated. The aim of this review was to evaluate the evidence of whether analgesics are capable of enhancing exercise performance and, if so, to what extent. Paracetamol has been suggested to improve endurance and repeated sprint exercise performance by reducing the activation of higher brain structures involved in pain and cognitive/affective processing. Nonsteroidal anti-inflammatory drugs affect both central and peripheral body systems, but investigation on their ergogenic effect on muscle strength development has provided equivocal results. The therapeutic use of glucocorticoids is indubitable, but clear evidence exists for a performance-enhancing effect after short-term oral administration. Based on the evidence presented in this review article, the ergogenic benefit of analgesics may warrant further consideration by regulatory bodies. In contrast to the aforementioned analgesics, there is a paucity of research on the use of opioids such as tramadol on sporting performance.

Introduction

There is little doubt that when exercise is performed above certain intensities, or over a prolonged period of time, it causes feeling of pain and discomfort. Sayings such as "no pain, no gain" often are heard in relation to both training and competition settings across a variety of different sports. Indeed, these feelings of exercise-induced pain have been shown to have a negative effect on training and performance [1]. As a consequence, there has been a trend for athletes from all levels and ages to use pharmacologic analgesics substances before training and competition up to 4-fold more than their age-matched general population [2]. The general term analgesic covers a variety of different pharmacologic substances, including nonsteroidal anti-inflammatory drugs (NSAIDs), nonopioid analgesics (such as paracetamol and others), weak opioids (for example, tramadol, codeine, or morphine [3]) and orally administered or injected glucocorticosteroids [4,5]. Indeed, paracetamol and NSAIDs are one of the most recurrent groups of pharmacological substances used by athletes, ranging from 11% up to 92% [6,7]. For instance, it is common for athletes with minor injuries to continue training, and even competing, by treating their minor health issues with analgesics [8].

The aforementioned negative association between pain and exercise capacity increases the likelihood of analgesic use as a method to increase the level of performance during competition [5,9]. Furthermore, the trends for more frequent use of analgesics in-competition versus out-competition, use of more than one drug at the same time, and administration of these medications at supratherapeutic dosages all suggest athletes may be using these analgesics as ergogenic aids [4,5]. Therefore, in contrast to the postexercise use of analgesics to accelerate recovery, there is potential for their prophylactic use as a potential performance-enhancing intervention. In comparison with what is known about the use of analgesics for treating sporting injury [10,11], much less is known about their effects on exercise-related physiology and performance [12-14]. However, because analgesics exert a pharmacologic action on key physiological systems related to exercise performance, a theoretical rationale exists whereby these drugs could provide a significant ergogenic effect.

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67. Huscher D, Thiele K, Gromnica-Ihle E, et al. Dose-related patterns of glucocorticoid-induced side effects. Ann Rheum Dis 2009;68:1119-1124.
68. Chatham WW, Kimberly RP. Treatment of lupus with corticosteroids. Lupus 2001;10:140-147.
69. Ueda N, Chihara M, Kawaguchi S, et al. Intermittent versus long-term tapering prednisolone for initial therapy in children with idiopathic nephrotic syndrome. J Pediatr 1988;112:122-126.
70. Liu X-Y, Liu Z-C, Sun Y-G, et al. Unidirectional cross-activation of GRPR by MOR1D uncouples itch and analgesia induced by opioids. Cell 2011;147:447-458.
71. Berridge CW, Schmeichel BE, España RA. Noradrenergic modulation of wakefulness/arousal. Sleep Med Rev 2012;16:187-197.
72. Schug SA. The role of tramadol in current treatment strategies for musculoskeletal pain. Ther Clin Risk Manag 2007;3:717-723.
73. Benson D. Tramadol abuse in the cycling peloton. Cyclingnews.com. 20013. Available at http://www.cyclingnews.com/news/tramadol-abuse-in-the-cycling-peloton. Accessed April 23, 2015.
74. Lipp J. Possible mechanisms of morphine analgesia. Clin Neuropharmacol 1991;14:131-147.
75. Benedetti F, Pollo A, Colloca L. Opioid-mediated placebo responses boost pain endurance and physical performance: Is it doping in sport competitions? J Neurosci 2007;27:11934-11939.
76. Sindrup SH, Brøsen K. The pharmacogenetics of codeine hypoalgesia. Pharmacogenetics 1995;5:335-346.
77. Brunton TL. On the use of codeine to relieve pain in abdominal disease. Br Med J 1888;1:1213-1214.
78. Kraemer WJ, Gómez A, Ratamess N, et al. Effects of VICOPROFEN and ibuprofen on anaerobic performance after muscle damage. J Sport Rehabil 2002;11:104-119.
79. VanHeest J, Stoppani J, Scheett TP, et al. Effects of ibuprofen and Vicoprofen® on physical performance after exercise-induced muscle damage. J Sport Rehabil 2002;11:224-234.
80. Langley PC, Patkar AD, Boswell KA, et al. Adverse event profile of tramadol in recent clinical studies of chronic osteoarthritis pain. Curr Med Res Opin 2010;26:239-251.
81. Perez-Lloret S, Videla AJ, Richaudeau A, et al. A multi-step pathway connecting short sleep duration to daytime somnolence, reduced attention, and poor academic performance: An exploratory cross-sectional study in teenagers. J Clin Sleep Med 2013;9:469-473.
82. WADA proposes Tramadol remains a monitored rather than a banned substance in 2015 | CyclingTips. Available at https://cyclingtips.com/2014/05/wada-proposes-tramadol-remains-a-monitored-rather-than-a-banned-substance-in-2015/. Accessed September 18, 2015.
83. Martinez-Silvestrini JA. Prescribing Medications for Pain and Inflammation. Edinburgh: W.B. Saunders; 2007.
84. Tscholl P, Feddermann N, Junge A, et al. The use and abuse of painkillers in international soccer: Data from 6 FIFA tournaments for female and youth players. Am J Sports Med 2009;37:260-265.
85. Orchard JW. Why glucocorticoids should be removed from the World Antidoping Agency's list of banned products. Br J Sports Med 2008;42:944-945.
86. Pigozzi F, Di Gianfrancesco A, Zorzoli M, et al. Why glucocorticosteroids should remain in the list of prohibited substances: A sports medicine viewpoint. Int J Immunopathol Pharmacol 2012;25:19-24.
87. WADA. The 2017 Monitoring Program. World Anti-Doping Agency. 2016. Available at https://wada-main-prod.s3.amazonaws.com/resources/files/wada-2017-monitoring-program-en.pdf. Accessed March 30, 2016.

Disclosure

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Original research

Tramadol effects on physical performance and sustained attention during a 20-min indoor cycling time-trial: A randomised controlled trial

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ABSTRACT

Objectives: To investigate the effect of tramadol on performance during a 20-min cycling time-trial (Experiment 1), and to test whether sustained attention would be impaired during cycling after tramadol intake (Experiment 2).
Design: Randomized, double-blind, placebo controlled trial.
Methods: In Experiment 1, participants completed a cycling time-trial, 120-min after they ingested either tramadol or placebo. In Experiment 2, participants performed a visual oddball task during the time-trial. Electroencephalography measures (EEG) were recorded throughout the session.
Results: In Experiment 1, average time-trial power output was higher in the tramadol vs. placebo condition (tramadol: 220 W vs. placebo: 209 W; $p < 0.01$). In Experiment 2, no differences between conditions were observed in the average power output (tramadol: 234 W vs. placebo: 230 W; $p > 0.05$). No behavioural differences were found between conditions in the oddball task. Crucially, the time frequency analysis in Experiment 2 revealed an overall lower target-locked power in the beta-band ($p < 0.01$), and higher alpha suppression ($p < 0.01$) in the tramadol vs. placebo condition. At baseline, EEG power spectrum was higher under tramadol than under placebo in Experiment 1 while the reverse was true for Experiment 2.
Conclusions: Tramadol improved cycling power output in Experiment 1, but not in Experiment 2, which may be due to the simultaneous performance of a cognitive task. Interestingly enough, the EEG data in Experiment 2 pointed to an impact of tramadol on stimulus processing related to sustained attention.
Trial registration: EudraCT number: 2015-005056-96.

1. Introduction

There is an increasing tendency to treat minor sporting injuries with the use of analgesic drugs in order that an athlete is able to continue training and competing. One of these "trending" analgesics is tramadol that is an opioid agonist and is used in the treatment of moderate to severe pain. Tramadol has a dual mechanism of action, being both an μ-opioid receptor agonist, and a serotonin and norepinephrine reuptake inhibitor.[1] Activation of the μ-opioid receptor agonist can cause analgesia and sedation. Likewise, by inhibiting serotonin and norepinephrine reuptake, tramadol seems to reduce pain perception.[1] Given the negative association between pain and exercise capacity, the prophylactic use of analgesic medication (also known as "painkillers") is relatively common to reduce pain in order to enhance sport performance.[2] Similar to other painkillers,[3] it is therefore possible that tramadol could improve

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to impair (behavioural) cognitive performance in the ability to maintain attention during exercise, although it may influence information processing as highlighted by EEG time-frequency data. It appears then that the presence of tramadol on the WADA's monitoring program seems reasonable as far as performance enhancement is concerned. Even though the present findings have to be considered with caution (as this is the first empirical approach to this issue), they open interesting venues for future research on this relevant topic.

Practical applications

Tramadol may improve cycling time-trial performance.

Tramadol influences information processing related to sustained attention at the brain level, although it was not translated into an impaired behavioural performance.

Anti-doping authorities may reconsider tramadol's status

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References

1. Bastami S, Haage P, Kronstrand R et al. Pharmacogenetic aspects of tramadol pharmacokinetics and pharmacodynamics after a single oral dose. *Forensic Sci Int* 2014; 238:125–132. http://dx.doi.org/10.1016/j.forsciint.2014.03.003.
2. Bastian B, Jetten J, Hornsey MJ et al. The positive consequences of pain: a biopsychosocial approach. *Pers Soc Psychol Rev* 2014; 18(3):256–279. http://dx.doi.org/10.1177/1088868314527831.
3. Mauger AR, Jones AM, Williams CA. Influence of acetaminophen on performance during time trial cycling. *J Appl Physiol* 2010; 108(1):98–104. http://dx.doi.org/10.1152/japplphysiol.00761.2009.
4. Ionescu AM, Manolescu BN, Popa R et al. Effects of tramadol treatment on aerobic exercise capacity in subjects with chronic non-specific low back pain. *Palestrica Third Millenn – Civiliz Sport* 2015; 16(3):214–218.
5. Mintzer MZ, Lanier RK, Lofwall MR et al. Effects of repeated tramadol and morphine administration on psychomotor and cognitive performance in opioid-dependent volunteers. *Drug Alcohol Depend* 2010; 111(3):265–268. http://dx.doi.org/10.1016/j.drugalcdep.2010.05.002.
6. Thürauf N, Fleischer WK, Liefhold J et al. Dose dependent time course of the analgesic effect of a sustained-release preparation of tramadol on experimental phasic and tonic pain. *Br J Clin Pharmacol* 1996; 41(2):115–123.
7. Robinson J, Germano S. The painkiller that cycling wants to see banned - WSJ. *Wall St J*. Available at: http://www.wsj.com/articles/the-painkiller-that-cycling-wants-to-ban-1476456216. Accessed 19 December 2016.
8. Loraschi A, Galli N, Cosentino M. Dietary supplement and drug use and doping knowledge and attitudes in Italian young elite cyclists. *Clin J Sport Med* 2013; 0(3):1–7. http://dx.doi.org/10.1097/JSM.0000000000000018.
9. Cary T. Team Sky deny Michael Barry's claim they ride on painkiller Tramadol - Telegraph. Available at: http://www.telegraph.co.uk/sport/othersports/cycling/10794325/Team-Sky-deny-Michael-Barrys-claim-they-ride-on-painkiller-Tramadol.html. Accessed 17 December 2016.
10. WADA. The 2017 Monitoring Program. World Anti-Doping Agency. Available at: https://wada-main-prod.s3.amazonaws.com/resources/files/wada-2017-monitoring-program-en.pdf.
11. Anti-doping Agency US. Tramadol Why Some Athletes and Experts Want It Banned. USADA. Available at: https://www.usada.org/tramadol-why-some-athletes-and-anti-doping-experts-want-it-banned/. Accessed 30 May 2017.
12. Perez-Lloret S, Videla AJ, Richaudeau A et al. A multi-step pathway connecting short sleep duration to daytime somnolence, reduced attention, and poor academic performance: an exploratory cross-sectional study in teenagers. *J Clin Sleep Med* 2013; 9(5):469–473. http://dx.doi.org/10.5664/jcsm.2668.
13. Faul F, Erdfelder E, Buchner A et al. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 2009; 41(4):1149–1160. http://dx.doi.org/10.3758/BRM.41.4.1149.
14. Lucía A, Rabadán M, Hoyos J et al. Frequency of the $V{\cdot}O_{2max}$ plateau phenomenon in world-class cyclists. *Int J Sports Med* 2006; 27(12):984–992. http://dx.doi.org/10.1055/s-2006-923833.
15. Sawaki R, Katayama J. Difficulty of discrimination modulates attentional capture for deviant information. *Psychophysiology* 2007; 44(3):374–382. http://dx.doi.org/10.1111/j.1469-8986.2007.00506.x.
16. Andrade E, Arce C, Seaone G. Adaptación al español del cuestionario «Perfil de los Estados de Ánimo» en una muestra de deportistas. *Psicothema* 2002; 14:708–713.
17. Simons CJP, Sambeth A, Krabbendam L et al. Auditory P300 and N100 components as intermediate phenotypes for psychotic disorder: familial liability and reliability. *Clin Neurophysiol* 2011; 122:1984–1990. http://dx.doi.org/10.1016/j.clinph.2011.02.033.
18. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to measure fatigue. *Psychiatry Res* 1990; 36:291–298. http://dx.doi.org/10.1016/0165-1781(91)90027-M.
19. Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 2004; 134(1):9–21. http://dx.doi.org/10.1016/j.jneumeth.2003.10.009.
20. Oostenveld R, Fries P, Maris E et al. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Comput Intell Neurosci* 2011; 2011. http://dx.doi.org/10.1155/2011/156869, 156869.
21. Hoffmann S, Falkenstein M. The correction of eye blink artefacts in the EEG: a comparison of two prominent methods. *PLoS One* 2008; 3(8):e3004. http://dx.doi.org/10.1371/journal.pone.0003004.
22. Pesarin F, Salmaso L. Wiley InterScience (online service), In: *Permutation Tests for Complex Data: Theory, Applications, and Software*. Wiley, 2010.
23. Pesarin F, Salmaso L. The permutation testing approach: a review. *Statistica* 2010; 70(4):481–509. http://dx.doi.org/10.6092/issn.1973-2201/3599.
24. Maris E, Oostenveld R. Nonparametric statistical testing of EEG- and MEG-data. *J Neurosci Methods* 2007; 164(1):177–190. http://dx.doi.org/10.1016/j.jneumeth.2007.03.024.
25. Foster J, Taylor L, Chrismas BCR et al. The influence of acetaminophen on repeated sprint cycling performance. *Eur J Appl Physiol* 2014; 114(1):41–48. http://dx.doi.org/10.1007/s00421-013-2746-0.
26. Peng W, Hu Y, Mao Y et al. Widespread cortical alpha-ERD accompanying visual oddball target stimuli is frequency but non-modality specific. *Behav Brain Res* 2015; 295:71–77. http://dx.doi.org/10.1016/j.bbr.2015.04.051.
27. McCormick A, Meijen C, Marcora S. Psychological determinants of whole-body endurance performance. *Sport Med* 2015; 45(7):997–1015. http://dx.doi.org/10.1007/s40279-015-0319-6.
28. Clayton MS, Yeung N, Cohen Kadosh R. The roles of cortical oscillations in sustained attention. *Trends Cogn Sci* 2015; 19(4):188–195. http://dx.doi.org/10.1016/j.tics.2015.02.004.
29. Friedel B. The effect of tramadol on the EEG and the electronystagmogram (author's transl). *Arzneimittelforschung* 1978; 28(1a):187–189.

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Original research

Effect of induced alkalosis on performance during a field-simulated BMX cycling competition

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ABSTRACT

Objectives: The aim of the present study was to test the effect of sodium bicarbonate ($NaHCO_3^-$) ingestion on performance during a simulated competition on a Bicycle Motocross (BMX) track.
Design: Double-blind cross-over study.
Methods: Twelve elite male BMX cyclists (age: 19.2 ± 3.4 years; height: 174.2 ± 5.3 cm; body mass: 72.4 ± 8.4 kg) ingested either NaHCO3- (0.3 $g.kg^{-1}$ body weight) or placebo 90 min prior to exercise. The cyclists completed three races in a BMX Olympic track interspersed with 15 min of recovery. Blood samples were collected to assess the blood acid-base status. Performance, cardiorespiratory, heart rate variability (HRV) as well as subjective variables were assessed.
Results: The main effect of condition ($NaHCO_3^-$ vs. placebo) was observed in pH, bicarbonate concentration and base excess ($p < 0.05$), with a significant blood alkalosis. No changes were found in time, peak velocity and time to peak velocity for condition ($p > 0.05$). The HRV analysis showed a significant effect of $NaHCO_3^-$ ingestion, expressed by the rMSSD30 (root mean square of the successive differences) ($p < 0.001$). There was no effect of condition on oxygen uptake, carbon dioxide production, or pulmonary ventilation ($p > 0.05$). Finally, there was no effect of condition for any subjective scale ($p > 0.05$).
Conclusions: We present here the first field condition study to investigate the effect of bicarbonate ingestion over performance in BMX discipline. The results showed that $NaHCO_3^-$-induced alkalosis did not improve performance in a simulated BMX competition in elite BMX cyclists, although future studies should consider the effects of NaHCO3- on autonomic function as a component of recovery.

1. Introduction

Numerous studies have demonstrated that increasing the extracellular buffer concentration via the oral ingestion of an alkaline solution such as sodium bicarbonate ($NaHCO_3^-$) may enhance human exercise performance.[1–3] These findings have maintained the practice of inducing alkalosis within the field of Sport Science for decades, although the physiological mechanism directly responsible for performance augmentation in humans is unknown. In the present study we focus on $NaHCO_3^-$ as a potential ergogenic aid to increase bicycle motocross (BMX) cycling performance via its effect on blood alkalosis, since $NaHCO_3^-$ is believed to mitigate fatigue through the attenuation of intramuscular acidity.[1,4]

Literature focusing on the effect of $NaHCO_3^-$ supplementation has shown contradictory findings. Some studies showed no effect on intermittent and all-out exercise,[5–7] despite significant blood alkalosis, while others have reported performance improvements.[8–10] Recent studies combining sodium bicarbonate ingestion with other substances, such as glucose or β-alanine, did not find significant benefits in exercise.[11,12] In general, during continuous dynamic exercises the performance has been usually improved whilst all-out exercise of shorter duration presents con-

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5. Zabala M, Peinado AB, Calderon FJ et al. Bicarbonate ingestion has no ergogenic effect on consecutive all out sprint tests in BMX elite cyclists. *Eur J Appl Physiol* 2011; 111:3127–3134.
6. Vanhatalo A, McNaughton LR, Siegler J et al. Effect of induced alkalosis on the power-duration relationship of "all-out" exercise. *Med Sci Sports Exerc* 2010; 42:563–570.
7. Siegler JC, Marshall PW, Bray J et al. Sodium bicarbonate supplementation and ingestion timing: does it matter? *J Strength Cond Res* 2012; 26:1953–1958.
8. Egger F, Meyer T, Such U et al. Effects of sodium bicarbonate on high-intensity endurance performance in cyclists: a double-blind, randomized cross-over trial. *PLoS One* 2014; 9:e114729.
9. Griffen C, Rogerson D, Ranchordas M et al. Effects of creatine and sodium bicarbonate coingestion on multiple indices of mechanical power output during repeated wingate tests in trained men. *Int J Sport Nutr Exerc Metab* 2015; 25:298–306.
10. Driller MW, Gregory JR, Williams AD et al. The effects of serial and acute $NaHCO_3$ loading in well-trained cyclists. *J Strength Cond Res* 2012; 26:2791–2797.
11. Price MJ, Cripps D. The effects of combined glucose-electrolyte and sodium bicarbonate ingestion on prolonged intermittent exercise performance. *J Sports Sci* 2012; 30:975–983.
12. Sale C, Saunders B, Hudson S et al. Effect of beta-alanine plus sodium bicarbonate on high-intensity cycling capacity. *Med Sci Sports Exerc* 2011; 43:1972–1978.
13. Requena B, Zabala M, Padial P et al. Sodium bicarbonate and sodium citrate: ergogenic aids? *J Strength Cond Res* 2005; 19:213–224.
14. Louis J, Billaut F, Bernad T et al. Physiological demands of a simulated BMX competition. *Int J Sports Med* 2013; 34:491–496.
15. Mateo M, Blasco-Lafarga C, Zabala M. Pedaling power and speed production vs. technical factors and track difficulty in bicycle motocross cycling. *J Strength Cond Res* 2011; 25:3248–3256.
16. Zabala M, Requena B, Sanchez-Munoz C et al. Effects of sodium bicarbonate ingestion on performance and perceptual responses in a laboratory-simulated BMX cycling qualification series. *J Strength Cond Res* 2008; 22:1645–1653.
17. Zinner C, Wahl P, Achtzehn S et al. Effects of bicarbonate ingestion and high intensity exercise on lactate and H(+)-ion distribution in different blood compartments. *Eur J Appl Physiol* 2011; 111:1641–1648.
18. Siegler JC, Midgley AW, Polman RC et al. Effects of various sodium bicarbonate loading protocols on the time-dependent extracellular buffering profile. *J Strength Cond Res* 2010; 24:2551–2557.
19. Buchheit M, Laursen PB, Ahmaidi S. Parasympathetic reactivation after repeated sprint exercise. *Am J Physiol Heart Circ Physiol* 2007; 293:H133–H141.
20. Goldberger JJ, Le FK, Lahiri M et al. Assessment of parasympathetic reactivation after exercise. *Am J Physiol Heart Circ Physiol* 2006; 290:H2446–H2452.
21. Mainwood GW, Worsley-Brown P. The effects of extracellular pH and buffer concentration on the efflux of lactate from frog sartorius muscle. *J Physiol* 1975; 250:1–22.
22. Bishop D, Edge J, Davis C et al. Induced metabolic alkalosis affects muscle metabolism and repeated-sprint ability. *Med Sci Sports Exerc* 2004; 36:807–813.
23. Bishop D, Claudius B. Effects of induced metabolic alkalosis on prolonged intermittent-sprint performance. *Med Sci Sports Exerc* 2005; 37:759–767.
24. Parkhouse WS, McKenzie DC. Possible contribution of skeletal muscle buffers to enhanced anaerobic performance: a brief review. *Med Sci Sports Exerc* 1984; 16:328–338.
25. Al Haddad H, Laursen PB, Chollet D et al. Reliability of resting and postexercise heart rate measures. *Int J Sports Med* 2011; 32:598–605.
26. Heck KL, Potteiger JA, Nau KL et al. Sodium bicarbonate ingestion does not attenuate the VO_2 slow component during constant-load exercise. *Int J Sport Nutr* 1998; 8:60–69.
27. Heil DP, Jacobson EA, Howe SM. Influence of an alkalizing supplement on markers of endurance performance using a double-blind placebo-controlled design. *J Int Soc Sports Nutr* 2012; 9, p8.
28. Mitchell TH, Abraham G, Wing S et al. Intravenous bicarbonate and sodium chloride both prolong endurance during intense cycle ergometer exercise. *Am J Med Sci* 1990; 300:88–97.
29. Zoladz JA, Szkutnik Z, Duda K et al. Preexercise metabolic alkalosis induced via bicarbonate ingestion accelerates VO_2 kinetics at the onset of a high-power-output exercise in humans. *J Appl Physiol* 2005; 98:895–904.

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The effects of transcranial direct current stimulation on objective and subjective indexes of exercise performance: A systematic review and meta-analysis

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ABSTRACT

Objective: To examine the effects of transcranial direct current stimulation (tDCS) on objective and subjective indexes of exercise performance.
Design: Systematic review and meta-analysis.
Data sources: A systematic literature search of electronic databases (PubMed, Web of Science, Scopus, Google Scholar) and reference lists of included articles up to June 2018.
Eligibility criteria: Published articles in journals or in repositories with raw data available, randomized sham-controlled trial comparing anodal stimulation with a sham condition providing data on objective (e.g. time to exhaustion or time-trial performance) or subjective (e.g. rate of perceived exertion) indexes of exercise performance.
Results: The initial search provided 420 articles of which 31 were assessed for eligibility. Finally, the analysis of effect sizes comprised 24 studies with 386 participants. The analysis indicated that anodal tDCS had a small but positive effect on performance $g = 0.34$, 95% CI [0.12, 0.52], $z = 3.24$, $p = .0012$. Effects were not significantly moderated by type of outcome, electrode placement, muscles involved, number of sessions, or intensity and duration of the stimulation. Importantly, the funnel plot showed that, overall, effect sizes tended to be larger in studies with lower sample size and high standard error.
Summary: The results suggest that tDCS may have a positive impact on exercise performance. However, the effect is probably small and most likely biased by low quality studies and the selective publication of significant results. Therefore, the current evidence does not provide strong support to the conclusion that tDCS is an effective means to improve exercise performance.

Introduction

Improving exercise performance represents the daily goal for many athletes. In the increasingly competitive context of sports, athletes are pressed to push their physical boundaries to run faster, increase power output, lift more weight or jump farther. As a consequence, athletes from all levels are willing to use cutting-edge methods to enhance their performance. Elevation training masks [1], iced garments [2] and virtual reality [3] are some remarkable examples. Another technique that is awakening interest in sports is transcranial direct current stimulation (tDCS) [4]. In fact, some companies have started to sell stimulation kits (sometimes in a do-it-yourself fashion) and professional and Olympic athletes have promoted them as an effective means to improve performance [5,6].

tDCS is a non-invasive brain stimulation technique that has been widely used in Neuroscience, as it has been deemed an effective and safe method to induce cortical changes by depolarizing (anodal) or hyperpolarizing (cathodal) neurons' resting membrane potential [7]. In a common tDCS set-up researchers use two electrodes; one electrode is the target electrode (i.e., deliver the weak current) and another is the reference electrode [8]. The reference electrode is normally placed on the contralateral brain area targeted or away of the head (e.g., in the shoulder) to avoid the delivery of current on the participant's scalp (i.e. extracephalically).

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https://doi.org/10.1016/j.brs.2018.12.002
1935-861X/

[32] Barwood MJ, Butterworth J, Goodall S, House JR, Laws R, Nowicky A, et al. The effects of direct current stimulation on exercise performance, pacing and perception in temperate and hot environments. Brain Stimulation 2016;9:842–9. https://doi.org/10.1016/j.brs.2016.07.006.

[33] Frazer A, Williams J, Spittles M, Rantalainen T, Kidgell D. Anodal transcranial direct current stimulation of the motor cortex increases cortical voluntary activation and neural plasticity. Muscle Nerve 2016;54:903–13. https://doi.org/10.1002/mus.25143.

[34] Lattari E, Andrade ML, Filho AS, Moura AM, Neto GM, Silva JG, et al. Can transcranial direct current stimulation improve the resistance strength and decrease the rating perceived scale in recreational weight-training experience? J Strength Condit Res 2016;30:3381–7. https://doi.org/10.1519/JSC.0000000000001457.

[35] Oki K, Mahato NK, Nakazawa M, Amano S, France CR, Russ DW, et al. Preliminary evidence that excitatory transcranial direct current stimulation extends time to task failure of a sustained, submaximal muscular contraction in older adults. J Gerontol Series A, Biol Sci Med Sci 2016;71:1109–12. https://doi.org/10.1093/gerona/glw011.

[36] Montenegro RA, Farinatti PTV, Lima D, F.m P, Okano AH, Menêses AL, et al. Motor cortex tDCS does not modulate perceived exertion within multiple-sets of resistance exercises. Isokinet Exerc Sci 2016;24:17–24. https://doi.org/10.3233/IES-150593.

[37] Okano AH, Machado DGS, Oliveira Neto L, Farias-Junior LF, Agrícola PMD, Arruda A, et al. Can transcranial direct current stimulation modulate psychophysiological response in sedentary men during vigorous aerobic exercise? Int J Sports Med 2017;38:493–500. https://doi.org/10.1055/s-0042-121897.

[38] Flood A, Waddington G, Keegan RJ, Thompson KG, Cathcart S. The effects of elevated pain inhibition on endurance exercise performance. PeerJ 2017;5, e3028. https://doi.org/10.7717/peerj.3028.

[39] Hazime FA, da Cunha RA, Soliaman RR, Romancini ACB, Pochini A de C, Ejnisman B, et al. Anodal transcranial direct current stimulation (tdcs) increases isometric strength of shoulder rotators muscles in handball players. Int J Sports Phys Ther 2017;12:402–7.

[40] Radel R, Tempest G, Denis G, Besson P, Zory R. Extending the limits of force endurance: stimulation of the motor or the frontal cortex? Cortex 2017. https://doi.org/10.1016/j.cortex.2017.09.026.

[41] Holgado DM, Zandonai T, Ciria LF, Zabala M, Hopker J, Sanabria D. tDCS over the left prefrontal cortex does not affect time-trial self-paced cycling performance: evidence from oscillatory brain activity and power output. BioRxiv 2018, 341388. https://doi.org/10.1101/341388.

[42] Lattari E, Campos C, Lamego MK, Passos de Souza SL, Neto GM, Rocha NB, et al. Can transcranial direct current stimulation improve muscle power in individuals with advanced resistance training experience? J Strength Condit Res 2017. https://doi.org/10.1519/JSC.0000000000001956.

[43] Lattari E, Rosa Filho BJ, Fonseca Junior SJ, Murillo-Rodriguez E, Rocha N, Machado S, et al. Effects on volume load and ratings of perceived exertion in individuals advanced weight-training after transcranial direct current stimulation. J Strength Condit Res 2018. https://doi.org/10.1519/JSC.0000000000002434.

[44] Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. Psychol Methods 2002;7:105–25.

[45] Conducting meta-analyses in R with the metafor package | viechtbauer | J Statist Software n.d. doi:10.18637/jss.v036.i03.

[46] Kimmerly DS, O'Leary DD, Menon RS, Gati JS, Shoemaker JK. Cortical regions associated with autonomic cardiovascular regulation during lower body negative pressure in humans. J Physiol 2005;569:331–45. https://doi.org/10.1113/jphysiol.2005.091637.

[47] Horvath JC, Forte JD, Carter O. Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: a systematic review. Neuropsychologia 2015;66:213–36. https://doi.org/10.1016/j.neuropsychologia.2014.11.021.

[48] Bikson M, Grossman P, Thomas C, Zannou AL, Jiang J, Adnan T, et al. Safety of transcranial direct current stimulation: evidence based update 2016. Brain Stimul 2016;9:641–61. https://doi.org/10.1016/j.brs.2016.06.004.

[49] Sanabria D. Are we ready to boost the riders' brain to enhance cycling performance? J Sci Cycl 2018;7:1–2. https://doi.org/10.28985/jsc.v7i1.395.

[50] Button KS, Ioannidis JPA, Mokrysz C, Nosek BA, Flint J, Robinson ESJ, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nat Rev Neurosci 2013;14:365–76. https://doi.org/10.1038/nrn3475.

[51] Munafò MR, Nosek BA, Bishop DVM, Button KS, Chambers CD, Percie du Sert N, et al. A manifesto for reproducible science. Nat Human Behav 2017;1:0021.

PLOS ONE

RESEARCH ARTICLE

Transcranial direct current stimulation (tDCS) over the left prefrontal cortex does not affect time-trial self-paced cycling performance: Evidence from oscillatory brain activity and power output

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Abstract

Objectives

To test the hypothesis that transcranial direct current stimulation (tDCS) over the left dorsolateral prefrontal cortex (DLPFC) influences performance in a 20-min time-trial self-paced exercise and electroencephalographic (EEG) oscillatory brain activity in a group of trained male cyclists.

Design

The study consisted of a pre-registered (https://osf.io/rf95j/), randomised, sham-controlled, single-blind, within-subject design experiment.

Methods

36 trained male cyclists, age 27 (6.8) years, weight 70.1 (9.5) Kg; $VO_{2max:}$ 54 (6.13) ml.min^{-1}. kg^{-1}, Maximal Power output: 4.77 (0.6) W/kg completed a 20-min time-trial self-paced exercise in three separate sessions, corresponding to three stimulation conditions: anodal, cathodal and sham. tDCS was administered before each test during 20-min at a current intensity of 2.0 mA. The anode electrode was placed over the DLPFC and the cathode in the contralateral shoulder. In each session, power output, heart rate, sRPE and EEG (at baseline and during exercise) was measured.

Results

There were no differences ($F = 0.31$, $p > 0.05$) in power output between the stimulation conditions: anodal (235 W [95%CI 222–249 W]; cathodal (235 W [95%CI 222–248 W] and

32. Horvath JC, Forte JD, Carter O. Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: A systematic review. Neuropsychologia. 2015; 66: 213–236. https://doi.org/10.1016/j.neuropsychologia.2014.11.021 PMID: 25448853

33. Veniero D, Vossen A, Gross J, Thut G. Lasting EEG/MEG Aftereffects of Rhythmic Transcranial Brain Stimulation: Level of Control Over Oscillatory Network Activity. Front Cell Neurosci. 2015; 9. https://doi.org/10.3389/fncel.2015.00477 PMID: 26696834

34. Minarik T, Berger B, Althaus L, Bader V, Biebl B, Brotzeller F, et al. The importance of sample size for reproducibility of tDCS effects. Frontiers in Human Neuroscience. 2016; 10: 453. https://doi.org/10.3389/fnhum.2016.00453 PMID: 27679568

35. Héroux ME, Loo CK, Taylor JL, Gandevia SC. Questionable science and reproducibility in electrical brain stimulation research. PLoS ONE. 2017; 12: 1–11. https://doi.org/10.1371/journal.pone.0175635 PMID: 28445482

36. Button KS, Ioannidis JPA, Mokrysz C, Nosek BA, Flint J, Robinson ESJ, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nature reviews Neuroscience. 2013; 14: 365–376. https://doi.org/10.1038/nrn3475 PMID: 23571845

37. Simonsohn U, Nelson LD, Simmons JP. P-curve: a key to the file-drawer. Journal of experimental psychology General. 2014; 143: 534–547. https://doi.org/10.1037/a0033242 PMID: 23855496

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RESEARCH ARTICLE

No evidence of the effect of cognitive load on self-paced cycling performance

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Abstract

Objectives

To test the hypothesis that cognitive load (low vs. high load) during a 20 min self-paced cycling exercise affects physical performance.

Design

A pre-registered (https://osf.io/qept5/), randomized, within-subject design experiment.

Methods

28 trained and experienced male cyclists completed a 20 min self-paced cycling time-trial exercise in two separate sessions, corresponding to two working memory load conditions: 1-back or 2-back. We measured power output, heart rate, RPE and mental fatigue.

Results

Bayes analyses revealed extreme evidence for the 2-back task being more demanding than the 1-back task, both in terms of accuracy ($BF_{10} = 4490$) and reaction time ($BF = 1316$). The data only showed anecdotal evidence for the alternative hypothesis for the power output ($BF_{10} = 1.52$), moderate evidence for the null hypothesis for the heart rate ($BF_{10} = 0.172$), anecdotal evidence for RPE ($BF_{10} = 0.72$) and anecdotal evidence for mental fatigue ($BF_{10} = 0.588$).

Conclusions

Our data **seem to** challenge the idea that self-paced exercise is regulated by top-down processing, given that we did not show clear evidence of exercise impairment (at the physical, physiological and subjective levels) in the high cognitive load condition task with respect to the low working memory load condition. The involvement of top-down processing in self-pacing the physical effort, however, cannot be totally discarded. Factors like the duration of the physical and cognitive tasks, the potential influence of dual-tasking, and the participants' level of expertise, should be taken into account in future attempts to investigate the role of top-down processing in self-paced exercise.

31. Borg G. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982; 14: 377–381. https://doi.org/10.1249/00005768-198205000-00012 PMID: 7154893

32. Jeffreys H. The Theory of Probability. 3rd ed. Oxford: Oxford Univ. Press; 1961.

33. Edwards AM, Polman RCJ. Pacing and awareness: brain regulation of physical activity. Sports Med Auckl NZ. 2013; 43: 1057–1064. https://doi.org/10.1007/s40279-013-0091-4 PMID: 23990402

34. McMorris T, Barwood M, Hale BJ, Dicks M, Corbett J. Cognitive fatigue effects on physical performance: A systematic review and meta-analysis. Physiol Behav. 2018; 188: 103–107. https://doi.org/10.1016/j.physbeh.2018.01.029 PMID: 29408319

35. Yogev-Seligmann G, Hausdorff JM, Giladi N. The role of executive function and attention in gait. Mov Disord. 2008; 23: 329–342. https://doi.org/10.1002/mds.21720 PMID: 18058946

36. Vera J, Perales JC, Jiménez R, Cárdenas D. A test-retest assessment of the effects of mental load on ratings of affect, arousal and perceived exertion during submaximal cycling. J Sports Sci. 2018; 36: 2521–2530. https://doi.org/10.1080/02640414.2018.1466848 PMID: 29688118

37. Pratt N, Willoughby A, Swick D. Effects of Working Memory Load on Visual Selective Attention: Behavioral and Electrophysiological Evidence. Front Hum Neurosci. 2011; 5. https://doi.org/10.3389/fnhum.2011.00057 PMID: 21716633

38. Abernethy B. Dual-task methodology and motor skills research: Some applications and methodological constraints. J Hum Mov Stud. 1988; 14: 101–132.

39. Jaeggi SM, Buschkuehl M, Perrig WJ, Meier B. The concurrent validity of the N-back task as a working memory measure. Memory. 2010; 18: 394–412. https://doi.org/10.1080/09658211003702171 PMID: 20408039

40. Schaefer S. The ecological approach to cognitive–motor dual-tasking: findings on the effects of expertise and age. Front Psychol. 2014; 5. https://doi.org/10.3389/fpsyg.2014.01167 PMID: 25352820

41. Martin K, Staiano W, Menaspà P, Hennessey T, Marcora S, Keegan R, et al. Superior Inhibitory Control and Resistance to Mental Fatigue in Professional Road Cyclists. PLOS ONE. 2016; 11: e0159907. https://doi.org/10.1371/journal.pone.0159907 PMID: 27441380

McMorris, T., & Hale, B. J. (2015). Is there an acute exercise-induced physiological/biochemical threshold which triggers increased speed of cognitive functioning? A meta-analytic investigation. *Journal of Sport and Health Science*, *4*(1), 4–13. https://doi.org/10.1016/j.jshs.2014.08.003

Oken, B. S., Salinsky, M. C., & Elsas, S. M. (2006). Vigilance, alertness, or sustained attention: Physiological basis and measurement. *Clinical Neurophysiology*, *117*(9), 1885–1901. https://doi.org/10.1016/j.clinph.2006.01.017

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, *2011*, 1–9. https://doi.org/10.1155/2011/156869

Parasuraman, R., & Mouloua, M. (1987). Interaction of signal discriminability and task type in vigilance decrement. *Perception & Psychophysics*, *41*(1), 17–22. https://doi.org/10.3758/BF03208208

Pesarin, F., & Salmaso, L. (2010). The permutation testing approach: A review. *Statistica*, *70*(4), 481.

Petruzzello, S. J., Hall, E. E., & Ekkekakis, P. (2001). Regional brain activation as a biological marker of affective responsivity to acute exercise: Influence of fitness. *Psychophysiology*, *38*(1), 99–106. https://doi.org/10.1111/1469-8986.3810099

Petruzzello, S. J., Landers, D. M., Hatfield, B. D., Kubitz, K. A., & Salazar, W. (1991). A meta-analysis on the anxiety-reducing effects of acute and chronic exercise: Outcomes and mechanisms. *Sports Medicine*, *11*(3), 143–182. https://doi.org/10.2165/00007256-199111030-00002

Pfurtscheller, G. (1992). Event-related synchronization (ERS): An electrophysiological correlate of cortical areas at rest. *Electroencephalography and Clinical Neurophysiology*, *83*(1), 62–69. https://doi.org/10.1016/0013-4694(92)90133-3

Pfurtscheller, G., & Aranibar, A. (1977). Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalography and Clinical Neurophysiology*, *42*(6), 817–826.

Pontifex, M. B., & Hillman, C. H. (2008). Neuroelectric measurement of cognition during aerobic exercise. *Methods*, *45*(4), 271–278. https://doi.org/10.1016/j.ymeth.2008.04.003

Sarter, M., Givens, B., & Bruno, J. P. (2001). The cognitive neuroscience of sustained attention: Where top-down meets bottom-up. *Brain Research Reviews*, *35*(2), 146–160. https://doi.org/10.1016/S0165-0173(01)00044-3

Sawaki, R., & Katayama, J. I. (2007). Difficulty of discrimination modulates attentional capture for deviant information. *Psychophysiology*, *44*(3), 374–382. https://doi.org/10.1111/j.1469-8986.2007.00506.x

Schmidt-Kassow, M., Heinemann, L. V., Abel, C., & Kaiser, J. (2013). Auditory–motor synchronization facilitates attention allocation. *NeuroImage*, *82*, 101–106. https://doi.org/10.1016/j.neuroimage.2013.05.111

Schneider, S., Brümmer, V., Abel, T., Askew, C. D., & Strüder, H. K. (2009). Changes in brain cortical activity measured by EEG are related to individual exercise preferences. *Physiology & Behavior*, *98*(4), 447–452. https://doi.org/10.1016/j.physbeh.2009.07.010

Thompson, T., Steffert, T., Ros, T., Leach, J., & Gruzelier, J. (2008). EEG applications for sport and performance. *Methods*, *45*(4), 279–288. https://doi.org/10.1016/j.ymeth.2008.07.006

Verburgh, L., Konigs, M., Scherder, E. J. A., & Oosterlaan, J. (2014). Physical exercise and executive functions in preadolescent children, adolescents and young adults: A meta-analysis. *British Journal of Sports Medicine*, *48*(12), 973–979. https://doi.org/10.1136/bjsports-2012-091441

Walsh, V. (2014). Is sport the brain's biggest challenge? *Current Biology*, *24*(18), R859–R860. https://doi.org/10.1016/j.cub.2014.08.003

Yagi, Y., Coburn, K. L., Estes, K. M., & Arruda, J. E. (1999). Effects of aerobic exercise and gender on visual and auditory P300, reaction time, and accuracy. *European Journal of Applied Physiology and Occupational Physiology*, *80*(5), 402–408. https://doi.org/10.1007/s004210050611

Yordanova, J., & Kolev, V. (1998). Event-related alpha oscillations are functionally associated with P300 during information processing. *NeuroReport*, *9*(14), 3159–3164. https://doi.org/10.1097/00001756-199810050-00007

Yordanova, J., Kolev, V., & Polich, J. (2001). P300 and alpha event-related desynchronization (ERD). *Psychophysiology*, *38*(1), 143–152. https://doi.org/10.1111/1469-8986.3810143

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OPINION
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"Brain-Doping," Is It a Real Threat?

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Since the term "Neurodoping" was introduced (Davis, 2013; Reardon, 2016), the use of transcranial direct current stimulation (tDCS) has gained popularity in Sports Science within a short space of time, based on the same straightforward logic: if exercise is to some extent determined by brain activity, then stimulating brain areas related to exercise should improve physical and sport performance. In fact, companies like Halo Sport claim that their "do-it-yourself" tDCS device has ergogenic effects and can increase sport and exercise performance (Reardon, 2016). In a recent review in Frontiers in Physiology, Angius et al. (2017) suggested that tDCS might have a positive effect on exercise capacity, although the mechanisms of that potential benefit were unknown. However, the expectations derived from those initial studies showing tDCS as an effective technique to increase exercise performance or reduce rate of perceived exertion (RPE), have left room for many others that do not seem to support the effectiveness of tDCS in the Sports science.

Indeed, recent meta-analyses have challenged the idea that tDCS can increase exercise performance or reduce RPE, mood or pain related to exercise (Holgado et al., 2018; Lattari et al., 2018a; Machado et al., 2018). For instance, based on the analysis of 36 effect sizes, Holgado et al. (2018)showed that the effect (if any) of tDCS on exercise performance is rather small ($g = 0.34$) and possibly inflated by methodological artifacts and selective publication. Similarly, the results of Machado et al. (2018) support the conclusion that tDCS has no effect on measures of muscle strength, although it may have a positive effect on cycling exercise. However, even this positive result seems to be entirely dependent on a single, low-quality study. Therefore, both Holgado et al. (2018) and Machado et al. (2018) reached the same conclusion: tDCS has little or no-effect on exercise performance. Moreover, it is worth mentioning that the chances of a publication bias in this topic are particularly high, that is, many other studies with null findings may not have been published or even sent for review (Holgado et al., 2018). So far, only one meta-analysis (Lattari et al., 2018a) has concluded that tDCS may be useful to increase performance. However, upon closer inspection, these results also seem to be grossly influenced by individual studies with unusually large effect sizes ($g = 3.56$ for Cogiamanian et al., 2007 and $g = 1.94$ for Lattari et al., 2018b), casting doubts on the reliability of these effects.

TABLE 1 | The most common placement of the tDCS' electrodes in the Sport Science research and its rationale.

Electrode placement	Rationale
Primary motor cortex (M1)	Increase M1 excitability to speed neural drive to active muscles Modulate pain perception
Prefrontal cortex	Changes in pacing behavior via executive functions, for example, by increasing inhibitory control capacity
Temporal cortex	Modulate the activity of the insular cortex Autonomic cardiac control Changes in self-perception and awareness of body sensations
Supplementary motor area	Reduce perceived exertion during exercise

The site of stimulation (**Table 1**), the fitness level of participants, the overly low sample sizes (average $N = 15$; which may lead to overestimation of effect sizes) and the likely ineffectiveness of the usual stimulation intensity (1–2 mA; cf. Vöröslakos et al., 2018) are key issues that would need to be considered in future research. Regarding stimulation intensity, recent studies have proposed that due to the high inter-individual variability in participants' electric fields, it seems that the most efficient approach to induce constable cortical changes would be to apply an individualized current intensity for each person (Esmaeilpour et al., 2018; Laakso et al., 2019). Indeed, the usual stimulation intensity does not seem to induce oscillatory brain electrical changes at rest or during exercise (e.g., Holgado et al., 2019; cf. Vöröslakos et al., 2018). Finally, the sham procedure might provide an additional source of variability, since without the appropriate procedure sham stimulation might have biological effects (Fonteneau et al., 2019).

In our opinion, the current evidence does not support the effectiveness of tDCS devices in the sport domain. It is therefore premature to make claims regarding the ergogenic benefits of tDCS and/or its potential thread as a novel doping tool. We believe, however, that this line of scientific enquiry could provide valuable knowledge if researchers endorse sound scientific practices (e.g., pre-registration, testing larger sample, multi-lab replications, etc.), to tackle issues like the role of stimulation intensity, the site of stimulation, and the inter-individual variability.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

Angius, L., Hopker, J., and Mauger, A. R. (2017). The ergogenic effects of transcranial direct current stimulation on exercise performance. *Front. Psychol.* 8:90. doi: 10.3389/fphys.2017.00090

Cogiamanian, F., Marceglia, S., Ardolino, G., Barbieri, S., and Priori, A. (2007). Improved isometric force endurance after transcranial direct current stimulation over the human motor cortical areas. *Eur. J. Neurosci.* 26, 242–249. doi: 10.1111/j.1460-9568.2007.05633.x

Davis, N. J. (2013). Neurodoping: brain stimulation as a performance-enhancing measure. *Sports Med.* 43, 649–653. doi: 10.1007/s40279-013-0027-z

Esmaeilpour, Z., Marangolo, P., Hampstead, B. M., Bestmann, S., Galletta, E., Knotkova, H., et al. (2018). Incomplete evidence that increasing current intensity of tDCS boosts outcomes. *Brain Stimul. Basic Transl. Clin. Res. Neuromodulation* 11, 310–321. doi: 10.1016/j.brs.2017.12.002

Fonteneau, C., Mondino, M., Arns, M., Baeken, C., Bikson, M., Brunoni, A. R., et al. (2019). Sham tDCS: a hidden source of variability? Reflections for further blinded, controlled trials. *Brain Stimul.* doi: 10.1016/j.brs.2018.12.977. [Epub ahead of print].

Holgado, D., Vadillo, M. A., and Sanabria, D. (2018). The effects of transcranial direct current stimulation on objective and subjective indexes of exercise performance: a systematic review and meta-analysis. *Brain Stimul.* 12, 242–250. doi: 10.1016/j.brs.2018.12.002

Holgado, D., Zandonai, T., Ciria, L. F., Zabala, M., Hopker, J., and Sanabria, D. (2019). Transcranial direct current stimulation (tDCS) over the left prefrontal cortex does not affect time-trial self-paced cycling performance: evidence from oscillatory brain activity and power output. *PLoS ONE* 14:e0210873. doi: 10.1371/journal.pone.0210873

Laakso, I., Mikkonen, M., Koyama, S., Hirata, A., and Tanaka, S. (2019). Can electric fields explain inter-individual variability in transcranial direct current stimulation of the motor cortex? *Sci. Rep.* 9:626. doi: 10.1038/s41598-018-37226-x

Lattari, E., Oliveira, B. R. R., Júnior, R. S. M., Neto, S. R. M., Oliveira, A. J., Neto, G. A. M., et al. (2018a). Acute effects of single dose transcranial direct current stimulation on muscle strength: A systematic review and meta-analysis. *PLoS ONE* 13:e0209513. doi: 10.1371/journal.pone.0209513

Lattari, E., Rosa Filho, B. J., Fonseca Junior, S. J., Murillo-Rodriguez, E., Rocha, N., Machado, S., et al. (2018b). Effects on volume load and ratings of perceived exertion in individuals advanced weight-training after transcranial direct current stimulation. *J. Strength Cond. Res.* doi: 10.1519/JSC.0000000000002434. [Epub ahead of print].

Machado, D. G. D. S., Unal, G., Andrade, S. M., Moreira, A., Altimari, L. R., Brunoni, A. R., et al. (2018). Effect of transcranial direct current stimulation on exercise performance: a systematic review and meta-analysis. *Brain Stimul.* doi: 10.1016/j.brs.2018.12.227. [Epub ahead of print].

Reardon, S. (2016). 'Brain doping' may improve athletes' performance. *Nat. News* 531, 283. doi: 10.1038/nature.2016.19534

Vöröslakos, M., Takeuchi, Y., Brinyiczki, K., Zombori, T., Oliva, A., Fernández-Ruiz, A., et al. (2018). Direct effects of transcranial electric stimulation on brain circuits in rats and humans. *Nat. Commun.* 9, 1–17. doi: 10.1038/s41467-018-02928-3

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LETTER TO THE EDITOR

Comment on "Review of WADA Prohibited Substances: Limited Evidence for Performance-Enhancing Effects"

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Dear Editor,

We read with great interest the review by Heuberger and Cohen entitled *"Review of WADA Prohibited Substances: Limited Evidence for Performance-Enhancing Effects"* [1]. In general terms, the authors summarise well the current lack of sufficient empirical evidence regarding the substances and methods included in the World Anti-Doping Agency (WADA) Prohibited List. However, although the review is well focused in 2018, we believe further information about the status of tramadol in 2019 is required. We write this letter to provide additional insights into the status of tramadol in cycling.

On 21 June, 2018, L'Union Cicliste International announced that tramadol will be banned in competition from the 1 March, 2019 [2]. According to the most recent report available from WADA, 4.3% of urine and blood sample analyses from cyclists contained tramadol [3]. Despite the L'Union Cicliste International banning tramadol in competition, WADA intends to keep tramadol on the monitoring programme until at least 2020 [4]. Notably, tramadol has been included in the monitoring programme since 2012 to detect potential patterns of abuse and to study its possible effects on performance and athletes' health. According to Heuberger and Cohen [1], there is scant evidence on the effect of tramadol on physical performance.

However, they omitted in their review a recent clinical trial from our laboratory in which we tested, for the first time, the effects of this substance in a group of cyclists at physical, cognitive and brain levels [5]. The purpose of the study (funded by WADA; reference 15C01DS) was to test the hypothesis that acute oral administration of tramadol would improve exercise performance during a 20-min cycling time trial in a group of cyclists (experiment 1). Furthermore, given the common side effects reported following the consumption of tramadol (e.g. drowsiness, somnolence and nausea [6]), we tested if sustained attention would be impaired during the 20-min time-trial while the participants performed an oddball sustained attention (cognitive) task (experiment 2). Tramadol might enhance cycling performance via its effect on effort and pain perception, but at the expense of reducing the ability to stay focused, i.e. to sustain attention, given that drowsiness and somnolence are commonly reported after tramadol ingestion. As tramadol will be prohibited in cycling from 2019, we believe these results are highly relevant for this topic of research.

In this double-blind, randomised, controlled within-subject experiment, participants ingested tramadol or placebo 120 min before the 20-min cycling time trial. The results of experiment 1, with a sample of 28 cyclists (19 male individuals, maximal power output: 4.72 W/kg and nine female individuals, maximal power output: 4.1 W/kg), revealed that tramadol improved performance by ~5% during a 20-min cycling time trial. Tramadol appeared to allow participants to achieve a higher power output without modifying the rate of perceived exertion. The methodology of experiment 2 was almost equivalent to that of experiment 1, except that participants (28 different male cyclists, maximal power output: 4.76 W/kg) completed a sustained attention (cognitive) task during the 20-min cycling time trial. The cognitive task consisted of a random presentation of a sequence of visual stimuli of a frequent blue circle (non-target), a small rare blue circle (target 1) and a rare square (target 2) on a computer screen. Participants were required to respond to both target 1 and target 2 and not to respond to the non-target. Interestingly, and contrary to the results observed in experiment 1,

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tramadol did not improve performance or impair sustained attention at the behavioural level compared to the placebo condition (i.e. neither response accuracy nor reaction time significantly differed between experimental conditions). Nonetheless, electrical brain activity measured during exercise following tramadol ingestion revealed an interesting pattern of results. We found a lower brain activity in the alpha frequency band linked to (task-relevant) stimulus processing in the tramadol recipients compared with placebo. Higher alpha activity has been deemed as an indicator of increased alertness [7]. In a study using a similar task, the reduction in the alpha frequency, observed when rare targets are presented, was interpreted to be a higher mental effort to detect infrequent targets [8].

Therefore, our results could point to the need for a greater cognitive resource allocation to detect infrequent targets in individuals receiving tramadol vs. placebo. The contradictory findings between experiment 1 and 2 might be explained by: (1) the simultaneous performance of a cognitive task in experiment 2 did not allow cyclists to allocate the same amount of resource to the physical test; and (2) the duration of the protocol. Fatigue could be an important factor that could mediate the impact of tramadol (i.e. the greater the fatigue, the larger the painkiller effect). Hence, at present, it is premature to state that tramadol enhances cycling performance or that it might have a negative effect on the ability to stay focused. Our laboratory is currently conducting a further trial to address some of the questions arising from the previous study.

In conclusion, whether tramadol will be finally included in the list of prohibited substances remains a question that WADA should address in the not-so-distant future supported by further empirical studies.

Compliance with Ethical Standards

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References

1. Heuberger JAAC, Cohen AF. Review of WADA prohibited substances: limited evidence for performance-enhancing effects. Sports Med. 2018;1:1. https://doi.org/10.1007/s40279-018-1014-1.
2. UCI. Inside UCI. http://www.uci.org/inside-uci/press-releases/the-management-committee-approves-agenda-2022-commits-to-greater-gender-equality-and-strengthens-its-ethics-regulations. Accessed 11 Nov 2018.
3. World Anti-Doping Agency. WADA publishes 2017 monitoring program figures (13 June 2018); 2018. https://www.wada-ama.org/en/media/news/2018-06/wada-publishes-2017-monitoring-program-figures. Accessed 11 Nov 2018.
4. World Anti-Doping Agency. The 2019 monitoring program; 2018. https://www.wada-ama.org/sites/default/files/wada_2019_french_monitoring_program.pdf. Accessed 23 Jan 2019.
5. Holgado D, Zandonai T, Zabala M, Hopker J, Perakakis P, Luque-Casado A, et al. Tramadol effects on physical performance and sustained attention during a 20-min indoor cycling time-trial: a randomised controlled trial. J Sci Med Sport. 2018;21:654–60.
6. Beakley BD, Kaye AM, Kaye AD. Tramadol, pharmacology, side effects, and serotonin syndrome: a review. Pain Physician. 2015;18:395–400.
7. Nielsen B, Nybo L. Cerebral changes during exercise in the heat. Sports Med. 2003;33:1–11.
8. Peng W, Hu Y, Mao Y, Babiloni C. Widespread cortical alpha-ERD accompanying visual oddball target stimuli is frequency but non-modality specific. Behav Res Med. 2015;295:71–7.

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ORIGINAL ARTICLE

WILEY PSYCHOPHYSIOLOGY SPR

Oscillatory brain activity during acute exercise: Tonic and transient neural response to an oddball task

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Abstract

Intense physical exercise exerts measurable changes at various physiological levels that are well documented in the literature. However, despite the key role of the brain in processing inputs from internal organ systems and the external environment to coordinate and optimize behavior, little is known about brain dynamics during exercise. The present study investigates tonic and transient oscillatory brain activity in a group of participants performing an oddball task during a single bout of aerobic exercise. Twenty young males (19–32 years) were recruited for two experimental sessions on separate days. EEG activity was recorded during a session of cycling at 80% (moderate-to-high intensity) of VO_{2max} (maximum rate of oxygen consumption) while participants responded to infrequent targets (red square and big blue circle) presented among frequent nontargets (small blue circle). This was compared to a (baseline) light intensity session (30% VO_{2max}) to control any potential effect of dual tasking (i.e., pedaling and performing the oddball task). A cluster-based nonparametric permutations test revealed an increase in power across the entire frequency spectrum during the moderate-to-high intensity exercise compared to light intensity. Furthermore, the more salient target (red square) elicited a lower increase in (stimulus-evoked) theta power in the 80% VO_{2max} than in the light intensity condition. Alpha and lower beta power decreased less in the standard trials (small blue circle) during the moderate-to-high exercise condition than in the light exercise condition. The present study unveils, for the first time, a complex brain activity pattern during vigorous exercise while attending to task-relevant stimuli.

KEYWORDS

brain function, brain rhythms, cluster analysis, EEG, exercise intensity, fitness, oddball

1 | INTRODUCTION

The brain plays a major role during strenuous physical exercise (e.g., cycling or running), managing afferent and efferent information from organs and body systems (Kayser, 2003) as well as monitoring external stimuli that may be potentially relevant for behavior (e.g., bumps, obstacles, cracks, etc.), making physical exercise a highly demanding cognitive task (Walsh, 2014). However, while the dynamics and regulatory mechanisms of body systems and organs like muscles, joints,

