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Neural basis for reduced executive performance with hypoxic exercise

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ABSTRACT

While accumulating evidence suggests positive effects of exercise on executive function, such effects vary with environment. In particular, exercise in a hypoxic environment (hypobaric or normobaric hypoxia), leading to decreased oxygen supply, may dampen or cancel such effects. Thus, we further explore the relation between the effects of hypoxic exercise on executive function and their underlying neural mechanisms by monitoring changes of cortical activation patterns using functional near-infrared spectroscopy (fNIRS). Fifteen healthy participants performed color-word Stroop tasks (CWST) before and after a 10 min bout of moderate-intensity exercise (50% $\dot{V}O_{2peak}$) under normoxic and hypoxic conditions (fraction of inspired oxygen (FIO_2) = 0.135). During the CWST, we monitored prefrontal activation using fNIRS. CWST performance under hypoxic conditions decreased compared with normoxic conditions. In addition, CWST-related activation in the left dorsolateral prefrontal cortex (DLPFC) was reduced after a bout of hypoxic exercise. There was statistically significant association between decreased CWST performance and activation in the left DLPFC. These results suggest that moderate exercise under normobaric hypoxic conditions has negative effects on executive function by reducing task-related activations in the DLPFC.

Introduction

Central command from the cerebral motor cortex, represented as cortical activation, causes muscle contraction during exercise by enhancing the drive of motor neurons. In addition to exercise-induced activation in the cerebral motor cortex, exercise leads to improved executive performance acting in lateral parts of the prefrontal cortex (Kujach et al., 2018; Byun et al., 2014; Hyodo et al., 2012; Yanagisawa et al., 2010). However, exercise might negatively affect physical or executive performance depending on various environmental factors. For example, maximum exercise (Chmura et al., 1994) or moderate-intensity exercise under hypoxic conditions (fraction of inspired oxygen (FIO_2) = 0.125; corresponding to an altitude of 4,000 m), which simulates mountaineering, leads to decreased executive function (Lefferts et al., 2016).

Regarding a potential reason for the impaired executive performance, cerebral hypoxia, which involves a substantial decrease of percutaneous arterial oxygen saturation (SpO_2), should be considered because hypoxic conditions greatly decrease SpO_2. In fact, it has been reported that memory and executive functions are reduced under severely hypoxic conditions at altitudes exceeding 4,000 m, where the blood-oxygen level drops causing cerebral hypoxia (McMorris et al., 2017; Taylor et al., 2016; Turner et al., 2015; Virués-Ortega et al., 2004). In addition, these global changes affect cerebral oxygenation in the prefrontal cortex even with mild- to moderate-intensity exercise under moderately hypoxic conditions (Ando et al., 2010; Subudhi et al., 2007). Intriguingly, transcranial magnetic stimulation studies have demonstrated that hypoxic-exercise-induced cerebral hypoxia is related to decreased cortical voluntary activation in the motor cortex (Goodall et al., 2012; Rasmussen et al., 2010). Likewise, hypoxic-exercise-induced cerebral hypoxia might further produce a negative effect on executive functions due to reduced prefrontal activations. However, the neural substrate of decreased executive function by hypoxic exercise is unclear. Thus, the present study aimed to clarify the effects of moderate exercise under normobaric hypoxic conditions on executive function and the underlying neural mechanisms in young adults.

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In order to explore the neural basis of a possible modulation of hypoxic-exercise-induced effects on executive functions, it is important to establish exercise and environmental conditions. Our previous study, combining a functional near-infrared spectroscopy (fNIRS) method and the color-word Stroop task (CWST), showed that acute moderate-intensity exercise improved executive function with increased task-related activation in the left dorsolateral prefrontal cortex (DLPFC) (Yanagisawa et al., 2010). fNIRS allows the assessment of cortical activation by measuring changes in hemodynamic responses, utilizing the tight coupling between neuronal activity and regional cerebral blood flow (Obrig and Villringer, 2003). Based on our previous findings, it is possible to postulate that reduced DLPFC activation might be related to exercise-induced executive impairment under hypoxic conditions.

To examine this hypothesis, we designed 2 experiments. In Experiment 1, we examined whether a bout of moderate-intensity exercise under normobaric hypoxic conditions ($FIO_2 = 0.135$; corresponding to an altitude of 3,500 m) leads to reduced executive function after exercise. We assessed the CWST performance before and after an acute bout of moderate physical exercise under normobaric hypoxic or normoxic conditions. Then, in Experiment 2, we examined the effect of a bout of moderate exercise under normobaric hypoxic conditions on executive function focusing on changes in cortical activation patterns. Using event-related multichannel fNIRS, we assessed the cortical activation patterns during the CWST before and after 10 min of moderate-intensity exercise or rest under hypoxic conditions.

Materials and methods

Participants

Fourteen right-handed young adults (mean age 23.4 ± 2.2 years (range 20–28 years); 1 female) participated in Experiment 1 and fifteen right-handed young adults (mean age 20.7 ± 2.1 years (range 18–25 years); 8 females) participated in Experiment 2. All participants were Japanese native speakers, healthy and naive to the experimental procedures for which they had volunteered. No participant stated a history of neurological, psychiatric or respiratory disorders or had a disease requiring medical care. All participants had normal or corrected-to-normal vision and normal color vision. This study was approved by the Institutional Ethics Committee of Tsukuba University, and was in accordance with the latest version of the Helsinki Declaration. All participants were asked to refrain from exercise and the consumption of alcohol and caffeine for at least 24 h prior to each experiment so as to control for outside factors that could affect cardiovascular and executive function.

Experiment 1

Experimental procedures

Experiment 1 was performed on three non-consecutive days. On the first day, participants underwent a graded exercise test to measure their peak oxygen uptake ($\dot{V}O_{2peak}$) and determine the appropriate individual intensity for moderate exercise, which was defined as 50% of a participant's $\dot{V}O_{2peak}$ based on the classification of physical activity intensity of the American College of Sports Medicine (ACSM, 2014). Detailed procedures for the graded exercise test are described in the pilot study 1 of supplementary materials. Participants practiced the CWST twice before the main experimental conditions. A few days after the first visit, two main experimental conditions, exercise under normobaric normoxic (NO) or normobaric hypoxic (HY) conditions, were conducted. All participants participated in both NO and HY conditions, each on separate days, with the order being counterbalanced across participants (Fig. 1A). In both conditions, participants underwent the CWST before and 15 min after 10 min of moderate-intensity exercise on a recumbent cycle ergometer at 60 revolutions per minute (rpm). This timeframe was chosen because non-cortically derived physiological parameters such as middle cerebral artery mean blood velocity (MCA V_{mean}) and forehead skin blood flow ($SkBF_{head}$) increase and SpO_2 and regional cerebral tissue oxygenation decrease with a 10 min bout of exercise at a moderate intensity and return to basal levels within 15 min (Supplementary Fig. 1).

In the HY condition, participants breathed hypoxic gas, which was mixture of 13.5% O_2 and 0.03% CO_2 in N_2 ($FIO_2 = 0.135$), through a mask that was connected to Douglas bags. In the NO condition, participants breathed the ambient air at sea level (normoxic gas), through a mask that was connected to Douglas bags. Expired air was exhausted directly outside the mask so that participants did not re-breathe it. The participants were exposed to hypoxic or normoxic gas from 10 min before the pre-Stroop session while sitting on the cycle ergometer so that all participants could perform the CWST after SpO_2 settled. Heart rate (HR) by heart rate monitor (V800, Polar Electro, Finland) and SpO_2 by a pulse

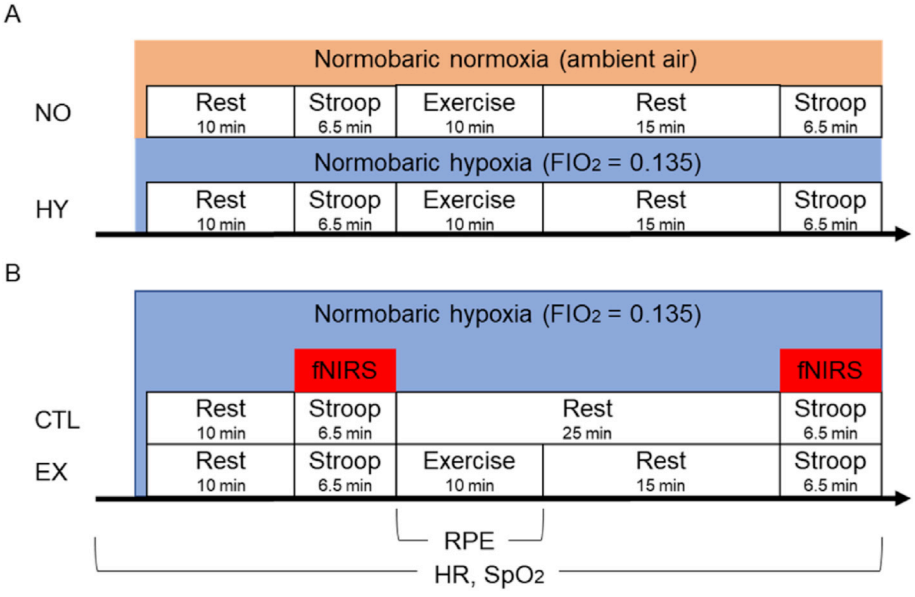

Fig. 1. (A) Experimental procedure for normobaric normoxic (NO) and hypoxic (HY) conditions of Experiment 1. (B) Experimental procedure for exercise (EX) and control (CTL) conditions of Experiment 2. Cortical hemodynamic changes were monitored with functional near-infrared spectroscopy (fNIRS) while participants performed the color-word Stroop task in Experiment 2.