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# Does moderate hypoxia alter working memory and executive function during prolonged exercise?

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## HIGHLIGHTS

- Little is known about how exercise under hypoxia alters cognitive function.
- We examined the combined effects of moderate hypoxia and prolonged exercise.
- Heart rate was matched during exercise between normoxia and moderate hypoxia.
- Moderate hypoxia did not impair working memory and executive function.
- Cognitive function improved during prolonged exercise under moderate hypoxia.

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## ABSTRACT

It has been suggested that acute exercise improves cognitive function. However, little is known about how exercise under hypoxia affects cognitive function. The purpose of this study was to determine if hypoxia alters working memory and executive function during prolonged exercise. Sixteen participants performed cognitive tasks at rest and during exercise under normoxia and hypoxia [fraction of inspired oxygen ($FIO_2$) = 0.15, corresponding to an altitude of approximately 2600 m]. The level of hypoxia was moderate. We used a combination of Spatial Delayed Response (Spatial DR) task and Go/No-Go (GNG) task, where spatial working memory and executive function are required. Working memory was assessed by the accuracy of the Spatial DR task, and executive function was assessed by the accuracy and reaction time in the GNG task. The participants cycled an ergometer for 30 min under normoxia and moderate hypoxia while keeping their heart rate (HR) at 140 beats/min. They performed the cognitive tasks 5 min and 23 min after their HR reached 140 beats/min. Moderate hypoxia did not alter the accuracy of the Spatial DR ($P = 0.38$) and GNG tasks ($P = 0.14$). In contrast, reaction time in the GNG task significantly decreased during exercise relative to rest under normoxia and moderate hypoxia ($P = 0.02$). These results suggest that moderate hypoxia and resultant biological processes did not provide sufficient stress to impair working memory and executive function during prolonged exercise. The beneficial effects on speed of response appear to persist during prolonged exercise under moderate hypoxia.



## 1. Introduction

The brain seems to be protected against hypoxia-induced reductions in arterial oxygen delivery at rest [29,34]. However, hypoxia potentially has detrimental effects on the central nervous system [1,28,40] and brain function [9,18]. Indeed, it has been suggested that cognitive function may be impaired by hypoxia [9,41,42]. The impairment appears to result from oxygen desaturation [9,41,42]. In contrast to the potential detrimental effects of hypoxia on cognitive function, there is a growing body of evidence to suggest that acute exercise improves cognitive function [7,24–26]. Hence, it follows that cognitive function during exercise under hypoxia may be determined by the balance between the beneficial effects of acute exercise and the detrimental effects of hypoxia. However, little is known about how cognitive function is altered during exercise under hypoxia. In particular, it is still unclear to what extent

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the effects of hypoxia and exercise on cognitive function are interactive. Understanding the factors that affect this balance may ultimately contribute to our understanding of the exercise–cognition interaction at high altitude.

Cognitive function has been assessed using the speed of response (reaction time) and accuracy in a cognitive task. A recent study demonstrated that a short bout of exercise under moderate hypoxia decreased reaction time without affecting accuracy [2]. This result indicates that the beneficial effects of acute exercise are still evident even during exercise under moderate hypoxia. However, there are two major limitations to being able to extend this finding to other conditions. The first limitation is related to the task used in that study, which was a modified version of the Go/No-Go (GNG) task [2]. Although the GNG task requires executive control, the GNG task used in the study was relatively easy to complete when it was performed alone. Task difficulty is one of the critical factors that affect exercise–cognition interaction [11,24]. Hence, we hypothesized that accuracy of demanding cognitive performance may be altered during exercise under moderate hypoxia. To elucidate this point, we used demanding cognitive tasks in which working memory and executive function are required. Physical activity at altitude (e.g. mountain climbing) requires higher cognitive ability under complex situations. It is essential to use demanding cognitive tasks in order to uncover the combined effects of exercise and hypoxia on performance.

The second limitation is related to the duration of exercise used in that study [2]. The exercise duration was only 10 min and the cognitive task was performed within this 10-min period. Recent reviews summarizing the effects of acute exercise on cognitive function indicate that the effects depend on the timing of the cognitive assessment [7,24]. These studies suggested that the improvement of cognitive function is more likely to occur when exercise duration is longer than 20 min. However, given that hypoxia potentially has detrimental effects on cognitive function [9,41,42], the effects of acute exercise on cognitive function may be different between normoxia and hypoxia as exercise is prolonged. Thus, we also tested if the beneficial effects of acute exercise are still observed during prolonged exercise under moderate hypoxia. Having a clearer understanding of the effects of prolonged exercise on cognitive function under hypoxia will provide further insight into exercise–cognition interaction.

The purpose of this study was to reveal how moderate hypoxia alters working memory and executive function during prolonged exercise. The findings from the present study will extend our knowledge about how exercise under hypoxia affects cognitive functioning.

## 2. Material and methods

### *2.1. Participants*

Sixteen male participants took part in the present study: mean ± SD, age = 23.0 ± 2.3 yr; height = 1.73 ± 0.07 m; body mass = 68.4 ± 7.2 kg; peak oxygen uptake = 45.7 ± 5.7 ml/kg × min. The participants were physically active and did not have any history of cardiovascular, cerebrovascular, or respiratory diseases. All participants gave written informed consent to participate. This study was approved by the ethics committee of Fukuoka University and was in accordance with the Declaration of Helsinki.

### *2.2. Cognitive task*

We used a laptop computer (Let's note CF-R4, Panasonic, Osaka, Japan) to present visual stimuli and record the data. In the present study, cognitive task was a combination of the Spatial Delayed Response (Spatial DR) task and the GNG task [14], where working memory and executive function are required. During the tasks, the participants faced a computer display at a viewing distance of approximately 80 cm while seated on a cycle ergometer (75XLII, COMBI Wellness, Tokyo, Japan). A portable ten-key pad and computer keyboards were horizontally situated above both sides of the handlebar. The participants pressed the ten-key with the right index finger (Spatial DR task) and pressed the shift button on the keyboard with the left index finger (GNG task). The cognitive tasks are summarized in Fig. 1. At the beginning of the Spatial DR task, the participants were asked to remember the location where the visual stimulus was presented. After that, the GNG task was started. On a Go-trial, participants released the shift button as quickly as possible. On a No-Go trial, participants continued pressing the shift button. After the GNG task, visual stimuli were presented at eight locations surrounding the fixation point. The participants pressed the button of the portable ten-key corresponding to the location they remembered (Fig. 1, bottom right). During the cognitive task, the participants received a correct and incorrect feedback tone.

The cognitive tasks continued until the participants completed 30 trials of both tasks. Time to complete the cognitive tasks was 303 ± 28 s. When the participants finished five successive trials in the GNG task, the relationship between the correct response and the figure was reversed for the next trial. After the next five successive trials were completed, the new pairs of figures were presented. In the Spatial DR task, we used the accuracy of the task to assess working memory and error trials were defined as incorrect responses to the remembered location. In the GNG task, executive function was evaluated using the accuracy and reaction time in the Go-trial. We defined error trials as omitting the response in the Go-trial, or an incorrect response in the No-Go trial. The accuracy of the Spatial DR and GNG tasks was calculated as the number of correct trials divided by the total number of the trials, respectively. In the GNG task, the participants did not know in advance when the correct response and the figure would be reversed or when the new pairs of figures would be presented. Therefore, we excluded trials immediately after the relationship between correct response and figure was reversed or one of a new pair of figures was presented when the accuracy of the task was calculated.

### *2.3. Experimental procedure*

The experiment was performed on two non-consecutive days. A few days before the first experiment, the participants completed practice blocks of the Spatial DR and GNG tasks at rest and during cycling, until they were familiar with the task and their performance became stable. On the days of the first experiment, the participants performed the cognitive task at rest, and during exercise under either normoxia [fraction of inspired oxygen ($FIO_2$) = 0.209] or normobaric hypoxia ($FIO_2$ = 0.15). A $FIO_2$ value of 0.15 corresponds to an altitude of approximately 2600 m at which physical activities are occasionally performed. The order of the normoxic and hypoxic conditions was randomly assigned and the participants were blinded to the respective air condition. At the beginning of the experiment, the participants were exposed to the normoxic or hypoxic gas for 10 min while sitting on the cycle ergometer. The participants breathed the gas through a mask that was connected to an environmental control chamber (FHC-20S, Fuji-ika Sangyo, Chiba, Japan). Thus, the participants breathed the gas coming from inside of the chamber. Inside the chamber, $CO_2$ was controlled at 0.03%. The air temperature and the relative humidity were set at 22 °C and 50%. Expired air was directly exhausted outside the mask so that the participants did not re-breathe the expired air.

After a 10-min exposure to the respective condition, the participants performed the cognitive task at rest while they rested on the cycle ergometer. One minute later, after they completed the first cognitive task, the participants started to cycle the ergometer. For the first 5 min, exercise intensity gradually increased at 30–32 W/min, and then increased at 20–21 W/min in a step-like manner until participants' heart rates (HR) reached 140 beats/min. An ear sensor, which was connected to the ergometer, continuously measured HR. When exercise is performed at the same absolute exercise intensity, HR increases to a greater extent during exercise under hypoxia compared to normoxia.