

# Effect of normobaric hypoxia exposure and exercise on attention

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#### HIGHLIGHTS

- The condition of hypoxia at rest did not change the performance indices related to attention.
- The condition of normobaric hypoxia on physical effort did not change the performance indices related to attention.
- · A Bayesian statistical approach was used.
- The determination of the effects of exposure to conditions of low oxygen concentration depend on the dose.

#### **ABBREVIATIONS**

BDNF Brain-derived neurothophic factor

BF<sub>10</sub> Bayes factor ES Effect size

FIO<sub>2.</sub> Inspired oxygen fraction H<sub>0</sub> Null hypothesis H<sub>1</sub> Alternative hypothesis HR Heart rate

O<sub>2</sub> Oxygen

PaO<sub>2</sub> Arterial oxygen pressure
SCWT Stroop Color-Word Test
SpO<sub>2</sub> Peripheral oxygen saturation
V<sub>PEAK</sub> Maximum velocity achieved
95% CI 95% confidence interval

**PUBLICATION DATA** 

Received 23 11 2021 Accepted 27 02 2022 Published 01 03 2022 **BACKGROUND:** Environment with low oxygen availability can have detrimental effects on cognitive abilities. Nevertheless, exercise can have beneficial effects on cognitive abilities, and these effects may vary with the environment. Therefore, it is important for the performance of individuals to understand the uncertainties about the conditions that can compromise cognitive function.

AIM: To identify which hypoxic conditions can cause attention disturbance.

**METHOD:** A total of fourteen volunteers ( $24.4 \pm 3.9$  years old;  $82.8 \pm 14.9$  kg weight;  $178.6 \pm 7.9$  cm height) participated in this single-blind, randomized, with a within-subjects design study. Participants completed an adapted version of the Stroop Color-Word Test (SCWT) before and after exposure in normoxia and hypoxia (FIO<sub>2</sub> = 0.209 and 0.138, respectively), in two conditions: (i) at rest for 30 minutes and (ii) under exhaustive effort. In addition to recording the SCWT time, peripheral oxygen saturation (SpO<sub>2</sub>) and heart rate (HR) were monitored, and hypoxia dose was calculated. The data were analyzed using a Bayesian statistical approach.

**RESULTS:** SCWT performance under hypoxic conditions showed no difference compared with exposure moments (before and after), as well as showed no difference compared with normoxic conditions. The SpO<sub>2</sub> in hypoxic conditions was significantly lower than in normoxia conditions, unlike HR, which revealed no difference. The hypoxia dose at rest and under exhaustive effort was 2.5 and 0.8 %.h, respectively.

**CONCLUSION:** Despite a drop in  $SpO_2$  and with hypoxia doses equivalent to 2.5 and 0.8 %.h, it was not possible to confirm differences in the indices related to attention. This indicates the existence of a minimum hypoxia dose to affect cognitive performance.

KEYWORDS: Normobaric hypoxia | Hypoxia dose | Exhaustive effort | Cognitive performance | Attention

# INTRODUCTION

The term "cognitive function" is related to a set of abilities that involves skills such as attention, information processing, learning, memory and problem solving <sup>1</sup>. Perceiving, associating, interpreting and responding are consequences that result from these abilities processed by different specific areas of the brain <sup>2</sup> and that allow the performance of tasks in different environments and at different levels of complexity, demonstrating the fundamental role of cognitive function in day-to-day life situations <sup>3</sup>.

It has been shown that, through increased cardiovascular, metabolic and neural activity, physical exercise facilitates core cognitive processes, increasing the speed and

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accuracy of responses to problem solving <sup>4,5,6</sup>. Although the mechanisms involved in this positive alteration have yet to be fully elucidated, increased release of neurotransmitters, as well as improvement in neurotransmission process and increased cerebral blood flow, may be involved in improving cognitive function <sup>1,7</sup>.

Among the mechanisms that may explain the cause-and-effect relationship between exercise and cognitive function, studies have identified that the level of arterial oxygen pressure (PaO<sub>2</sub>) is a strong predictor of cognitive performance <sup>6,7</sup>, indicating that oxygen availability is a key element for sustaining this relationship. Under hypoxic conditions, reduced PaO<sub>2</sub>, as well as cerebral O<sub>2</sub> desaturation, have been indicated as disruptors of cognitive function <sup>8</sup>.

The performance of simple and complex tasks, as well as memory, attention, and reaction time, appear to be susceptible to hypoxic conditions <sup>9</sup>. In addition, reduced cerebral oxygenation induced during exercise in hypoxic conditions may be related to lower voluntary activation in the motor cortex <sup>10</sup>. This indicates that the increased cerebral blood flow generated by exercise, added to the increased muscle demand, is unable to compensate for the lack of oxygen <sup>7</sup>.

Kim et al. <sup>11</sup> found that, after five hours of exposure to a hypoxic environment, four of which were spent at rest and one was spent doing cycling exercise, there was a decline in cognitive performance and a reduction in cerebral oxygenation. Similarly, the study conducted by Morrison et al. <sup>12</sup> revealed that single sprint sets performed in hypoxic conditions resulted in compromised cognitive function.

In contrast, when evaluating working memory and reaction time after 30 minutes of submaximal exercise in hypoxic conditions, Komiyama et al. <sup>13</sup> concluded that this was not sufficient to cause any detrimental effect on cognitive function. Likewise, Ando et al. <sup>14</sup> demonstrated that even at different levels of hypoxia and different exercise intensities, cognitive function was not altered by oxygen unavailability, despite the reduction in cerebral oxygenation.

Therefore, the lack of agreement on the conditions that can compromise cognitive function is notorious. Accordingly, the rationale for this work is the importance of understanding the effects of an environment of low oxygen availability, as well as when added to exercise, on cognitive abilities, since the performance of athletes in training camps or in competitions depends on cognitive resources, because attention is the most relevant information processing capacity for a good development of learning, as also for the best decision making. Additionally, the dependence on cognitive resources also applies to productivity and absence of errors and accidents of residents and workers such as mountain quides, military personnel and aircraft pilots.

Thus, this study identified which hypoxic conditions can cause disturbance in cognitive function, especially attention. For this, at first, in Study 1, the situation of 30 minutes of exposure to hypoxia at rest was defined from the fact that this acute condition (<1 hour) is enough to cause instability in neural activity <sup>15</sup>. In Study 2, the situation of an exhaustive effort in hypoxia was presented according to the basis that this context induces a reduction in cerebral oxygenation <sup>16</sup>.

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### **METHODS**

## **Participants**

A total of 14 healthy men participated in this study, nine of them participated in Study 1 (24.7  $\pm$  4.6 years old; 82.6  $\pm$  17.3 kg weight; 177.4  $\pm$  7.1 cm height) and five took part in Study 2 (23.4  $\pm$  0.9 years old; 80  $\pm$  10 kg weight; 180  $\pm$  9.3 cm height). Participants who declared to be physically active were included, and those who reported having traveled to altitudes above 1500 meters in the last 6 months or indicated having difficulty related to color vision were excluded. The participants were only confirmed for the study after signing an informed consent form, and all procedures conducted in this study are in accordance with the Ethics Committee for Research with Human Beings of the School of Physical Education and Sport of Ribeirão Preto of the University of São Paulo (grant number: 3.600.074/13353919.0.0000.5659) and with the Declaration of Helsinki.

### Normobaric Normoxia and Normobaric Hypoxia

In both Studies 1 and 2, the participants breathed through a unidirectional mask (Air safety, Brazil) attached to a flexible tube, whose opposite end was connected to a tent (2 meters wide, 3 meters long and 2 meters high; Colorado Altitude Training Tent  $^{TM}$ , USA), connected to a hypoxia generator (CAT-430  $^{TM}$ , Altitude Control Technologies, USA). The O<sub>2</sub> concentration monitoring inside the tent was done with an O<sub>2</sub> sensor (Oxygen Sensor R-17MED, Teledyne Analytical Instruments, USA). For the experimental procedure described below, an altitude of approximately 3353 meters with an inspired oxygen fraction of 13.8% (FIO<sub>2</sub> = 0.138) was simulated for the hypoxic condition. For normoxic condition, participants performed the same procedures, but breathing air containing 20.9% O<sub>2</sub> (FIO<sub>2</sub> = 0.209).

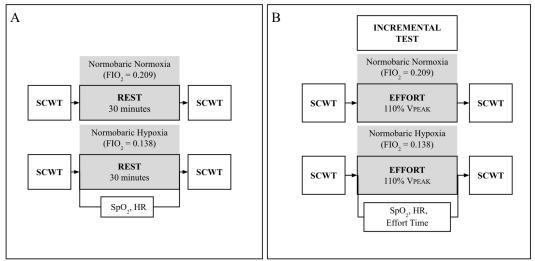
#### **Experimental Procedures**

Participants came to the laboratory (531 meters above sea level, 22°C controlled temperature) on two different days for Study 1, which investigated the effects of normobaric hypoxia on attention. For this, the participants performed the adapted Stroop Color-Word Test (SCWT) before and after a 30-minute exposure at rest under the conditions of normoxia and hypoxia, in a random manner. During the 30 minutes, in both conditions, peripheral oxygen saturation (SpO<sub>2</sub>) data were collected using a portable finger pulse oximeter (OxyWatch MD300C1, ChoiceMMed), and heart rate (HR) was measured using a frequency meter (Polar Team System, Polar Electro OY, Kempele, Finland) connected to the Elite HRV app (Figure 1).

Study 2, in turn, lasted a total of three days, investigating the effects of normobaric hypoxia combined with physical exercise on attention. On the first day, the participants did an incremental test to determine the maximum velocity achieved ( $V_{PEAK}$ ). On the second and third days, randomly, an effort was done until voluntary exhaustion at 110%  $V_{PEAK}$  in normoxia and in hypoxia. Before and immediately after the efforts, the participants were subjected to the same adapted SCWT test, and the HR and  $SpO_2$  data were noted every 30 seconds, along with the total effort time (Figure 1).

It is important to indicate that this study employed a single-blind, randomized with a within-subjects design.

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**Figure 1**. Experimental procedure of Study 1 (A) and experimental procedure of Study 2 (B). SCWT: Stroop Color-Word Test; SpO<sub>2</sub>: peripheral oxygen saturation; HR: heart rate; V<sub>PEAK</sub>: maximum velocity achieved in the incremental test.

## The Stroop Color-Word Test (SCWT)

The SCWT is a cognitive test that prioritizes the attention phase of information processing as a form of successful interaction with the environment <sup>17</sup>. For this study, the adapted test consisted of four columns, each containing 12 words and letters in Portuguese referring to different colors (red, blue, yellow, and green) written both in the same colors and in black (Figure 2). Previously, the participants were instructed on the development of the test: (i) each column should be done separately, but in order and with no big intervals between them; (ii) the words should be read aloud continuously and as fast and accurately as possible; (iii) if the participants made a mistake, they should start reading the column again; (iv) for the "Word Condition" (first column) and "Word-color Condition" (second column), the written words should be read, and for the "Color-letter Condition" (third column) and "Interference Condition" (fourth column), the painted colors to be named; and finally (v) the test performance would be determined using a chronometer to time the reading of the words, per column, starting with the participants first visual contact and concluding when they read the last word. The effect of learning was minimized by changing the orders of the words for each column, every day the SCWT was applied.

#### **Incremental Test**

The maximal incremental test, done on a treadmill (Super ATL, Imbrahmed, Brazil), was preceded by a five-minute warm-up at 7 km h<sup>-1</sup>. Three minutes after the warm-up, starting at a speed of 8 km h<sup>-1</sup>, the intensity was increased by 1 km h<sup>-1</sup> every two minutes, until the participants judged themselves incapable of continuing the effort. They were verbally encouraged to delay interruption to the maximum. The V<sub>PEAK</sub> was considered the highest velocity reached in the incremental test, and if the participant was unable to complete the time of the last stage, the equation adapted from Kuipers et al. <sup>18</sup> was used.

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WC	W-CC	C-LC	IC
vermelho	azul	XXX	verde
verde	verde	mmmm	azul
amarelo	vermelho	hhh	amarelo
vermelho	azul	SSSSSSSS	verde
azul	amarelo	hhhhhhh	vermelho
verde	azul	XXX	azul
azul	verde	SSSS	amarelo
vermelho	vermelho	XXXXXX	vermelho
amarelo	amarelo	mmm	verde
azul	verde	SSSSS	vermelho
amarelo	amarelo	mmmm	azul
verde	vermelho	hhhhhhh	amarelo

**Figure 2**. The Stroop Color-Word Test (SCWT) used to estimate cognitive performance. WC: Word Condition (first column), W-CC: Word-color Condition (second column), C-LC Color-letter Conditions (third column), IC: Interference Condition (fourth column).

### **Hypoxia Dose Estimation**

Hypoxia dose was estimated for each participant considering that, for the same  $FIO_2$ , participants may present different reductions in  $SpO_2$ , and increased  $O_2$  demand due to the exercise, as well as lower  $O_2$  availability under hypoxic conditions. This hypoxia dose was assumed to be the exposure time in hours (t) multiplied by the reduction in  $SpO_2$ , accepting a resting  $SpO_2$  value of 98%. Thus, hypoxia dose =  $(98 - average\ SpO_2)\ x$  t, as adapted from Millet et al. <sup>19</sup>.

#### **Statistical Analysis**

The statistical analyses were done with JASP software (Amsterdam, Netherlands), version 0.12.2. Data are described as average  $\pm$  standard deviation. A Bayesian statistical approach with a previous hypothesis (Cauchy = 0.707) was used to provide probabilistic statements to explore the recorded data. The Bayesian paired t-test was used to analyze the difference between the SCWT times in the pre- and post-intervention moments in hypoxia, both at rest and for exhaustive effort, as well as to analyze the difference in post-and pre-intervention SCWT times ( $\Delta$  SCWT) between hypoxia and normoxia exposure. The average values of physiological SpO<sub>2</sub> and HR were also examined. Data normality was confirmed using Shapiro-Wilk's test (p < 0.05); the Bayesian Student paired t-test was chosen for a parametric approach and the Bayesian Wilcoxon test was used for a non-parametric approach. Mean standardized effect size (ES) and 95% confidence interval (95% CI) were also calculated, and interpreted by Cohen <sup>20</sup> as negligible < 0.2, small 0.2 - 0.5, medium 0.5 - 0.8, and large > 0.8. Evidence for the null hypothesis (H<sub>0</sub>), which determines that the difference between the conditions is equal to zero, was defined as Bayes factor

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 $(BF_{10})$  < 1, and evidence for the alternative hypothesis  $(H_1)$  was established as Bayes factor  $(BF_{10})$  > 1. The strength of evidence category was also mentioned according to the qualitative interpretation made by Lee and Wagenmakers 21:  $BF_{10}$  > 1 = anecdotal evidence for  $H_1$ ;  $BF_{10}$  > 3 = moderate evidence for  $H_1$ ;  $BF_{10}$  > 10 strong evidence for  $H_1$ ;  $BF_{10}$  > 30 = very strong evidence for  $H_1$ ;  $BF_{10}$  > 100 = extreme evidence for  $H_1$ ; while  $BF_{10}$  < 1 = anecdotal evidence for  $H_0$ ;  $BF_{10}$  < 1/30 = very strong evidence for  $H_0$ ;  $BF_{10}$  < 1/100 = extreme evidence for  $H_0$ .

### RESULTS

#### Study 1

The physiological SpO<sub>2</sub> and HR variables are presented in Figure 3. Based on the hypoxia dose calculation for each participant, the average hypoxia dose obtained for a total time of 30 minutes at rest was 2.5 %.h ( $\pm$  1.2). The Bayesian analysis related to the difference between average SpO<sub>2</sub> in normoxia, of 97.1% ( $\pm$  0.9), and in hypoxia, of 92.9% ( $\pm$  2.5), demonstrated a probability favoring H<sub>1</sub> (BF<sub>10</sub> = 74.870), with the strength of evidence considered as very strong. In contrast, the analysis related to average HR in normoxia, of 65.6 bpm ( $\pm$  8.6), and in hypoxia, of 65.6 bpm ( $\pm$  11.1), favored H<sub>0</sub> (BF<sub>10</sub> = 0.322), with moderate strength of evidence.

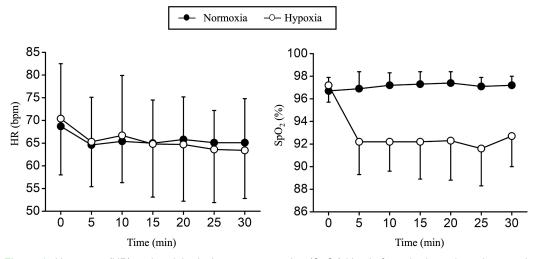
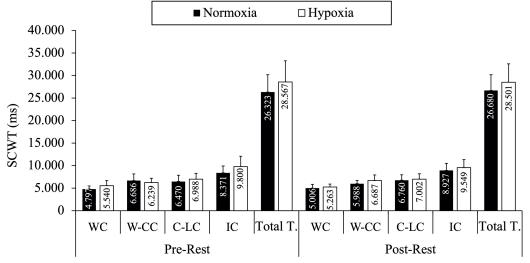


Figure 3. Heart rate (HR) and peripherical oxygen saturation (SpO<sub>2</sub>) kinetic from the hypoxic and normoxic conditions during 30 minutes at rest.

The average times recorded while doing the SCWT at rest in normoxia and hypoxia, for each column and each moment, are reported in Figure 4. The Bayesian analysis related to the differences between the pre- and post-intervention moments in the hypoxic condition identified a greater probability in favor of  $H_0$ , with the strength of evidence considered anecdotal for word-color (BF $_{10}$  = 0.788), interference (BF $_{10}$  = 0.365) conditions, and for the total time (BF $_{10}$  = 0.378), and moderate for word (BF $_{10}$  = 0.323) and color-letter (BF $_{10}$  = 0.322) conditions. Estimates of ES and 95% CI between the moments in each column are presented in Table 1.

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**Figure 4**. Average descriptive data on cognitive performance in the condition of hypoxia and normoxia at rest for the pre- and post-moments. SCWT: Stroop Color-Word Test, in milliseconds; WC: word condition, W-CC: word-color condition, C-LC: color-letter condition, IC: interference condition; Total T.: total time.

**Table 1.** Data from the Bayesian paired t-test corresponding to the pre- vs. post- 30-minute moments in the hypoxic condition at rest.

SCWT (ms)	ES	95% CI	BF <sub>10</sub>	Strength of Evidence
Word Condition	I -0.02 Negligible	-0.64; 0.61	0.323	Moderate for H₀
Word-color Condition	-0.52 Medium	-1.20; 0.20	0.788	Anecdotal for H <sub>0</sub>
Color-letter Condition	-0.01 Negligible	-0.66; 0.64	0.322	Moderate for H₀
Interference Condition	0.18 Negligible	-0.48; 0.84	0.365	Anecdotal for H <sub>0</sub>
Total T.	0.29 Small	-0.77; 0.41	0.378	Anecdotal for H <sub>0</sub>

SCWT (ms): Stroop Color-Word Test, in milliseconds; ES: effect size; 95% CI: 95% confidence interval; BF<sub>10</sub>: Bayesian factor; H<sub>0</sub>: null hypothesis; Total T.: total time

A probability in favor of  $H_0$  was confirmed for the average  $\Delta$  SCWT, with the strength of evidence considered anecdotal for word (BF<sub>10</sub> = 0.580), color-letter (BF<sub>10</sub> = 0.349) and interference (BF<sub>10</sub> = 0.423) conditions, and a probability in favor of  $H_1$  for word-color condition, but with anecdotal strength of evidence (BF<sub>10</sub> = 1.363). Individual  $\Delta$  SCWT for each column, for each condition, as well as their respective average values are shown in Figure 5.

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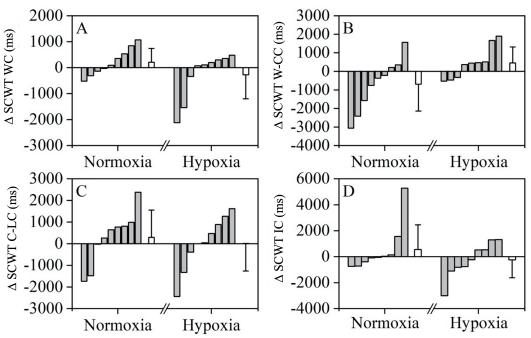


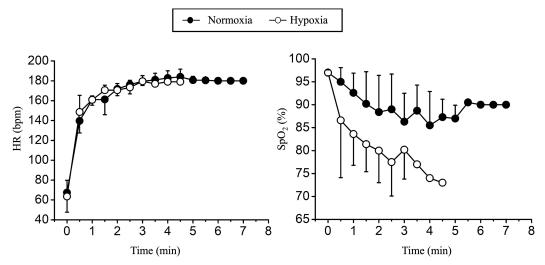
Figure 5. Individual difference in post- pre-intervention SCWT times (individual  $\Delta$  SCWT: gray columns) and average difference in post- pre-intervention SCWT times (average  $\Delta$  SCWT: white column) for each column in normoxic and hypoxic conditions at rest.  $\Delta$ : difference post- pre-intervention SCWT times; SCWT: Stroop Color-Word Test, in milliseconds; WC: word condition, W-CC: word-color condition, C-LC: color-letter condition, IC: interference condition.

# Study 2

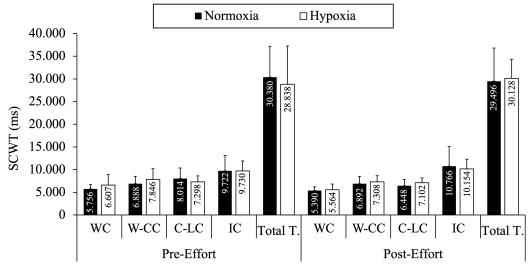
The physiological SpO<sub>2</sub> and HR variables are presented in Figure 6. Based on the hypoxia dose calculation for each participant, considering the time sustained during each exhaustive effort, average hypoxia dose was 0.8 %.h ( $\pm$  0.4). The Bayesian analysis related to the difference between the average SpO<sub>2</sub> in normoxia, of 90.1% ( $\pm$  5.9), and in hypoxia, of 83.5% ( $\pm$  6.1), confirmed a probability favoring H<sub>1</sub> (BF<sub>10</sub> = 1.425), with the strength of evidence evaluated as anecdotal. In contrast, the analysis related to the average HR in normoxia, of 160.5 bpm ( $\pm$  8.1), and in hypoxia, of 157.1 bpm ( $\pm$  6.8), pointed in favor of H<sub>0</sub> (BF<sub>10</sub> = 0.810), with anecdotal strength of evidence.

The average times recorded while doing the SCWT in combination with the exhaustive effort in normoxia and hypoxia, for each column and each moment, are reported in Figure 7. The Bayesian analysis related to the differences between the pre- and post-intervention moments in the hypoxic condition identified a greater probability for  $H_0$ , with anecdotal strength of evidence for word-color (BF $_{10}$  = 0.449), color-letter (BF $_{10}$  = 0.536), interference (BF $_{10}$  = 0.426) conditions, and for total time (BF $_{10}$  = 0.420), and a greater probability for  $H_1$  with anecdotal strength of evidence for word (BF $_{10}$  = 1.978) condition. Estimates of ES and the 95% CI between the moments in each column are presented in Table 2.

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**Figure 6**. Heart rate (HR) and peripherical oxygen saturation (SpO<sub>2</sub>) kinetic from the hypoxic and normoxic conditions during the exhaustive effort.



**Figure 7.** Average descriptive data on cognitive performance in the condition of hypoxia and normoxia at exhaustive effort for the pre- and post-moments. SCWT: Stroop Color-Word Test, in milliseconds; WC: word condition, W-CC: word-color condition, C-LC: color-letter condition, IC: interference condition; Total T.: total time.

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**Table 2.** Data from the Bayesian paired t-test at the pre- vs. post-exercise moments done until exhaustion in the hypoxic condition.

SCWT (ms)	ES	95% CI	BF <sub>10</sub>	Strength of Evidence
Word Condition	1.97 Large	-0.15; 4.05	1.978	Anecdotal for H <sub>1</sub>
Word-color Condition	0.25 Small	-0.66; 1.12	0.449	Anecdotal for H₀
Color-letter Condition	0.40 Small	-0.54; 1.29	0.536	Anecdotal for H₀
Interference Condition	-0.18 Negligible	-1.06; 0.71	0.426	Anecdotal for H₀
Total T.	-0.16 Negligible	-1.04; 0.73	0.420	Anecdotal for H <sub>0</sub>

SCWT (ms): Stroop Color-Word Test, in milliseconds; ES: effect size; 95% CI: 95% confidence interval; BF<sub>10</sub>: Bayesian factor; H<sub>0</sub>: null hypothesis; H<sub>1</sub>: alternative hypothesis; Total T.: total time.

A probability in favor of  $H_0$  was confirmed for average  $\Delta$  SCWT, with the strength of evidence considered anecdotal for word (BF<sub>10</sub> = 0.499), word-color (BF<sub>10</sub> = 0.452) and interference (BF<sub>10</sub> = 0.541) conditions, and a probability in favor of  $H_1$  for color-letter condition, but with anecdotal strength of evidence (BF<sub>10</sub> = 1.839). Individual  $\Delta$  SCWT for each column, for each condition, as well as their respective average values, are shown in Figure 8.

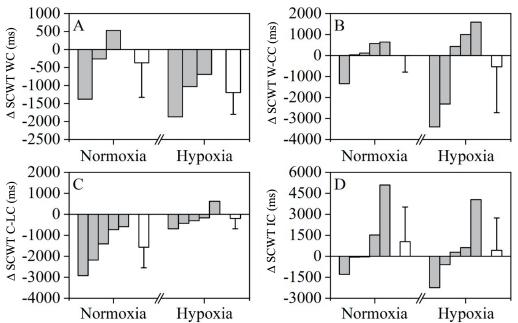


Figure 8. Individual difference in post- pre-intervention SCWT times (individual  $\Delta$  SCWT: gray columns) and average difference in post- pre-intervention SCWT times (average  $\Delta$  SCWT: white column) for each column in normoxic and hypoxic conditions with exhaustive effort.  $\Delta$ : difference post- pre-intervention SCWT times; SCWT: Stroop Color-Word Test, in milliseconds; WC: word condition, W-CC: word-color condition, C-LC: color-letter condition, IC: interference condition.

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## DISCUSSION

The purpose of this study was to investigate the effects of exposure to an environment with low oxygen availability at rest and in a situation combined with physical exercise on cognitive performance. The main finding was that neither exposure to normobaric hypoxia at rest for 30 minutes, nor to normobaric hypoxia while doing exhaustive exercise, resulted in any alteration in attention performance.

These results were inconsistent with those found in previous studies that have demonstrated that hypoxic condition has detrimental effects on cognitive function  $^{11,12,22,23}$ . Williams et al.  $^{24}$  found a correlation between alterations in cognitive performance, cerebral oxygenation levels, and oxygen saturation levels. In fact, the present study reported that the reduction in SpO<sub>2</sub> was significant in the hypoxic condition, but there was no alteration in cognitive function.

One possible explanation for such divergences between the findings of this study and those in the literature may be related to the hypoxia dose, or the "severity of hypoxia" <sup>5</sup>. Bouak et al. <sup>22</sup> observed cognitive performance in memory and executive function tasks at various altitudes, and they found a reduction in memory performance in moderate hypoxia environments (3048 and 3658 meters) and in executive function performance in severe hypoxia environment (4267 meters), while no alteration was observed in the mild hypoxia environment (2438 meters).

According to data published by Bouak et al. <sup>22</sup>, hypoxia doses for severe, moderate, and mild hypoxia conditions after moderate exercise (60W for 7 minutes, in a total of 62 minutes of exposure) were 21.8 %.h, 16.6 and 11.3%.h, and 7.2 %.h, respectively. In the present investigation, 30 minutes of hypoxia exposure with an average peripheral oxygen saturation of 92.9%, as well as combined hypoxia exposure and exhaustive effort with an average peripheral oxygen saturation of 83.5%, and, therefore, with hypoxia doses equivalent to 2.5 %.h and 0.8 %.h, did not result in the deterioration of cognitive attention performance.

The hypoxia doses observed in resting hypoxia conditions (Study 1) and during exhaustive effort (Study 2) were 88.5% and 96.3% lower than the doses calculated for severe hypoxia and 77.9% and 92.9% lower than those for moderate hypoxia (3048 meters) in the study of Bouak et al. <sup>22</sup>. Possibly, due to that, the performance in the attention test was not altered with hypoxia at rest nor when combined with exercise. Considering this, it is plausible to propose that there is a minimum hypoxia "threshold" dose in which deterioration in the attention indices are observed.

Physiologically, the existing competition for the little oxygen available and the heterogeneous distribution of cerebral blood flow may affect areas associated with cognitive performance <sup>25</sup>. Turner et al. <sup>26</sup> state that attention, processing speed, and memory functions depend on neural signals originating from the frontal cortex, whose region appears to be more vulnerable to oxygen availability. Also, for the same reason, the results of the study of Périard et al. <sup>27</sup> demonstrated, using recorded electroencephalographic frequency data, that reduced mental readiness activity, and synaptic transmission appear to be limited due to the sensitivity of neural activity.

In contrast, interestingly and curiously, recent studies <sup>28,29</sup> argue that exposure to hypoxia can also have beneficial effects, acting on neuroprotection by stimulating the synthesis of neurotrophins, such as brain-derived neurotrophic factor (BDNF), allowing a

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positive interpretation even in a health perspective. Furthermore, it is already argued that physical exercise alone adds to cognitive function <sup>1</sup>, however, the elegant systematic review and meta-analysis by Jung et al. <sup>3</sup> add that exercise performed under hypoxia conditions has favorable effects on cognitive abilities. Therefore, hypoxia dose can determine the competitive relationship between deleterious effects and the beneficial effects of hypoxia on the impact of cognitive performance.

Another possible explanation may be related with the mode of exercise and its intensity combined with the severity of hypoxia, which can create a conflicting relationship with the distribution of cerebral blood flow, as there is an undeniable dispute between skeletal muscles and the brain, causing redistribution of oxygen supply to essential areas for homeostatic functions <sup>23</sup>. There are also indications of cognitive performance domain types which may not be sensitive to hypoxia <sup>12</sup>. McMorris et al. <sup>7</sup> and Ando et al. <sup>25</sup> clarify that central executive tasks tend to be more negatively affected by hypoxia than non-executive tasks.

However, the experimental procedure presented indicates some limitations. The small number of participants can influence the interpretation of results due to the lack of statistical significance. In addition, SpO<sub>2</sub> could have been monitored throughout the cognitive test, which could have justified the scattered results with strength of anecdotal evidence favoring H<sub>1</sub>. Nevertheless, this study contributes to the understanding that it is possible that the beneficial or detrimental effects of exposure to hypoxia on cognitive performance, and even on health, are dependent on several factors, including "hypoxia severity". Therefore, further studies, investigating potential mechanisms and the most sensitive variables that could clarify this relationship between cognitive performance and hypoxia, in addition to confirming the influence of exercise, are pressing.

### CONCLUSION

In summary, 30 minutes of hypoxia and exhaustive exercise in hypoxia with hypoxia doses equivalent to 2.5 and 0.8 %.h do not significantly alter the indices related to attention, suggesting the existence of a minimum hypoxia dose threshold.

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### **ACKNOWLEDGEMENTS**

We would like to thank all the participants who spared no efforts to carry out all the stages of this study. We also would like to thank the School of Physical Education and Sport

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of Ribeirão Preto at the University of São Paulo (EEFERP / USP) and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for all the support offered.

Citation: Andreossi JC, Ribeiro FA, Bertucci DR, Papoti M. (2022). Effect of Normobaric Hypoxia Exposure and Exercise on Attention. *Brazilian Journal of Motor Behavior*, 16(1):11-25.

**Editors**: Dr Fabio Augusto Barbieri - São Paulo State University (UNESP), Bauru, SP, Brazil; Dr José Angelo Barela - São Paulo State University (UNESP), Rio Claro, SP, Brazil; Dr Natalia Madalena Rinaldi - Federal University of Espírito Santo (UFES), Vitória, ES, Brazil.

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Funding: The financial assistance to purchase the equipment used was supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), São Paulo, Brazil (grant number: 16/12781-5).

Competing interests: The authors have declared that no competing interests exist.

DOI: https://doi.org/10.20338/bjmb.v16i1.270

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