Acute physical exercise under hypoxia improves sleep, mood and reaction time

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**A B S T R A C T**

This study aimed to assess the effect of two sessions of acute physical exercise at 50% VO2peak performed under hypoxia (equivalent to an altitude of 4500 m for 28 h) on sleep, mood and reaction time. Forty healthy men were randomized into 4 groups: Normoxia (NG) (n = 10); Hypoxia (HG) (n = 10); Exercise under Normoxia (ENG) (n = 10); and Exercise under Hypoxia (EHG) (n = 10). All mood and reaction time assessments were performed 40 min after awakening. Sleep was reassessed on the first day at 14 h after the initiation of hypoxia; mood and reaction time were measured 28 h later. Two sessions of acute physical exercise at 50% VO2peak were performed for 60 min on the first and second days after 3 and 27 h, respectively, after starting to hypoxia. Improved sleep efficiency, stage N3 and REM sleep and reduced wake after sleep onset were observed under hypoxia after acute physical exercise. Tension, anger, depressed mood, vigor and reaction time scores improved after exercise under hypoxia. We conclude that hypoxia impairs sleep, reaction time and mood. Acute physical exercise at 50% VO2peak under hypoxia improves sleep efficiency, reversing the aspects that had been adversely affected under hypoxia, possibly contributing to improved mood and reaction time.

**1. Introduction**

Atmospheric pressure and, consequently, the partial pressure of inspired oxygen (PO2) decrease at high altitudes. As a result, a reduction in the PO2 of arterial blood and body tissues is classically described. Accordingly, physiological and behavioral changes can occur in both animal models and humans [1].

A study performed by Gao et al. [2] showed that individuals living at an altitude of 4500 m for 5 years exhibited an impairment of mood, sleep quality and cognitive functions, and exposure to hypobaric hypoxia (3700–5100 m for 5 days) was found to promote negative changes in mood and reaction time [3]. Roach et al. [4] conducted a study on a mountain at 5000 m and demonstrated that exposure to hypoxia for 16 days impaired reaction time. Such chronic impairments may occur within the first few hours after exposure. Reductions in sleep efficiency, slow-wave sleep and REM sleep were observed under simulated altitude in a normobaric chamber for 24 h. Several mood parameters were impaired, with depressed mood, anger, fatigue, and vigor scores being observed [5]. It is clear that hypoxia causes physiological and behavioral impairments, which may increase the risk of accidents and death [6]. Furthermore, hypoxia can cause health problems such as hypertension and cardiovascular diseases [7].

Therefore, different strategies are employed to minimize the damage caused by hypoxia, which include dietary supplements, medications and the use of oxygen [8,9,10,11,12,13,14]. However, physical exercise was the strategy used in the present study.
Physical exercise performed under normoxia has been described as an approach that improves many body functions, including sleep, mood and cognition [15,16,17,18,19,20]. To our knowledge, however, the effects of physical exercise performed under hypoxia on sleep, mood and cognition have not been simultaneously evaluated.

Therefore, this study aimed to evaluate the effect of two sessions of acute physical exercise at 50% VO2peak performed under hypoxia equivalent to an altitude of 4500 m for 28 h on sleep, mood and reaction time. Based on the knowledge that acute physical exercise performed under normoxia benefits health in general, we hypothesized that the two sessions at 50% of VO2peak performed under hypoxia might reverse the impairment of sleep, mood and reaction time.

2. Methods

2.1. Participants

Before participating in the study, the volunteers were informed about all possible risks associated with the experimental procedure. The study was approved by the Research Ethics Committees of the Federal University of São Paulo - São Paulo Hospital (Universidade Federal de São Paulo - Hospital São Paulo) (# 1110-1108) and followed the guidelines established in the Declaration of Helsinki of 1964. Data were collected at the Psychobiology and Exercise Research Center (Centro de Estudos em Psicobiologia e Exercício-CEPE) between 2012 and 2014.

The study was advertised by electronic and print media. Interested individuals came into contact with the researcher, who recruited personally.

The sample consisted of 40 healthy male volunteers who were randomized into 4 groups: Normoxia (NG) (n = 10); Hypoxia (HG) (n = 10); Exercise under Normoxia (ENG) (n = 10); and Exercise under Hypoxia (EHG) (n = 10). The characteristics of the sample were described as the mean ± standard deviation, as shown in Table 1. All volunteers performed specific activities, which included strength training, cycling and running two or three times a week for at least 6 months. The volunteers typically went to bed at approximately 22:00 pm and woke up at 07:00 am. All participants were males aged 20 to 30 years. The exclusion criteria were as follows: the use of tobacco, alcohol, illicit drugs, or any others drugs; exposure to hypoxic conditions in the last 12 months; and heart problems or sleep disorders, including obstructive sleep apnea, periodic limb movement disorder (PLMD), or any other alterations that could increase sleep fragmentation.

Of the 40 volunteers, 38 completed the study. One subject was excluded due to the presence of acute mountain sickness symptoms during the experiment, including severe headache and nausea [21]; these complaints were substantiated according to the Lake Louise consensus criteria [22]. The other subject was excluded because of the occurrence of obstructive sleep apnea, detected through polysomnography.

2.2. Experimental design and procedures

During the first visit to the laboratory, the volunteers underwent a resting and effort electrocardiogram. On the second visit, they underwent a spirometry test to determine VO2peak. On the third visit, the volunteers were subjected to the experimental procedure corresponding to the group to which they were randomly assigned.

The entire experiment was conducted in a double-blind manner for the hypoxic condition. The time at which sleep, mood and reaction time were assessed in all groups as well as the time of hypoxia exposure are shown in Fig. 1. Exposure to hypoxia was initiated at 8 am on the first day at an FiO2 of 20.9% O2, equivalent to sea level. This fraction was gradually reduced for 1.5 h until reaching an FiO2 of 13.5% O2, corresponding to a simulated altitude of 4500 m. The simulation was completed on the second day at 12:10 am, when FiO2 was returned to sea level conditions.

One week after the first adaptation polysomnographic evaluation was performed, the volunteers arrived in the laboratory to sleep, after which the second polysomnographic assessment was conducted under normoxia.

On the first day, the volunteers awoke at 7:00 am, and after 40 min, the mood and reaction time assessments were conducted. The ENG and EHG groups performed one physical activity session. The third polysomnographic evaluation was carried out on the second night, 10 h after the first acute physical exercise session and 14 h after the initiation of hypoxic conditions.

On the second day, the volunteers awoke at 7:00 am after remaining under hypoxia for 23 h, and the second acute physical exercise session began after 27 h. The second mood and reaction time assessment was performed immediately after the end of the second acute physical exercise session. This timeline was employed to observe the response of mood and reaction time after the second standardized exercise session under the same conditions as the first day.

At the end of the experiment, the volunteers were dismissed when no clinical symptoms that might prevent them from leaving the laboratory were observed.

Throughout the experiment, each volunteer remained alone in the adapted room with a bathroom for 28 h after the initiation of hypoxic conditions at sea level. The volunteers had free access to television, the internet, books, magazines and a cell phone during the experimental period [5]. The investigators observed the volunteers from outside the room using a closed-circuit camera system to ensure that the volunteers did not nap during the day.

Four meals were served in the course of the experiment: breakfast (7:10 am to 7:30 am), lunch (12:20 pm to 1:20 pm), afternoon snack (4 pm to 4:20 pm) and dinner (7:20 pm to 8:20 pm), totaling 1784.80 ± 227.0 kcal/day. The Harris–Benedict equation [23] was

### Table 1

Descriptive statistics for the sample.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Normoxia Mean ± (SD)</th>
<th>Hypoxia Mean ± (SD)</th>
<th>Exercise under normoxia Mean ± (SD)</th>
<th>Exercise under hypoxia Mean ± (SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.2 ± (3.1)</td>
<td>23.3 ± (2.2)</td>
<td>26.1 ± (3.2)</td>
<td>24.1 ± (2.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>69.2 ± (1.4)</td>
<td>67.5 ± (8.2)</td>
<td>71.4 ± (10.3)</td>
<td>72.1 ± (11.2)</td>
<td>0.83</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.78 ± (0.05)</td>
<td>1.75 ± (0.08)</td>
<td>1.75 ± (0.07)</td>
<td>1.78 ± (0.07)</td>
<td>0.83</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.1 ± (7.3)</td>
<td>22.3 ± (2.1)</td>
<td>23.1 ± (1.2)</td>
<td>22.1 ± (1.3)</td>
<td>0.56</td>
</tr>
<tr>
<td>HRMax</td>
<td>191.2 ± (3.1)</td>
<td>194.3 ± (8.2)</td>
<td>186.3 ± (11.2)</td>
<td>197.3 ± (6.2)</td>
<td>0.30</td>
</tr>
<tr>
<td>VO2peakmax</td>
<td>47.1 ± (4.2)</td>
<td>47.4 ± (6.2)</td>
<td>44.4 ± (5.4)</td>
<td>49.1 ± (3.1)</td>
<td>0.39</td>
</tr>
<tr>
<td>Educational level (years)</td>
<td>15.00 ± (1.9)</td>
<td>16.4 ± (1.26)</td>
<td>15.30 ± (1.76)</td>
<td>16.5 ± (1.19)</td>
<td>0.11</td>
</tr>
<tr>
<td>Energy expenditure (kcal)</td>
<td>1757.2 ± (141.1)</td>
<td>1718.1 ± (158.2)</td>
<td>1751.1 ± (160.5)</td>
<td>1855.8 ± (140.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Carbohydrate (%)</td>
<td>61.5 ± (1.2)</td>
<td>62.3 ± (1.0)</td>
<td>60.8 ± (1.5)</td>
<td>63.3 ± (1.7)</td>
<td>0.20</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>23.6 ± (0.5)</td>
<td>24.2 ± (0.6)</td>
<td>24.9 ± (0.7)</td>
<td>23.3 ± (0.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>14.2 ± (0.09)</td>
<td>13.9 ± (0.4)</td>
<td>14.7 ± (0.8)</td>
<td>14.0 ± 0.52</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Results are reported as the mean ± (standard deviation). Comparisons were performed using one-way ANOVA. BMI = body mass index; HR = maximum heart rate. The significance level was set at p ≤ 0.05.
Fig. 1. Summary of the experimental design for all groups: NG, HG, ENG and EHG; Acronyms: Polysomnography = PSG.
used to calculate the daily energy expenditure and balanced kcal distribution in the four meals for each volunteer. The diet composition of the meals is described according to System Brand Brasil de Dietoterapia software, version 35.11.

2.3. Normobaric chamber

The study was conducted in a room equipped for altitude simulations reaching up to 4500 m, which corresponds to a barometric pressure of 433 mmHg (normobaric chamber, CAT – Colorado Altitude Training®/12 CAT-Air Unit, Louisville, CO, USA). The sessions in the normobaric chamber were initiated under normoxic conditions (FiO2 of 20.9% O2) and gradually increased to a simulated altitude of 4500 m, which corresponds to an FiO2 of 13.5% O2.

2.4. Physiological assessments

2.4.1. Oxygen saturation

A finger pulse oximeter (Fingertrip® - California, USA) was used to measure oxygen saturation (SaO2%). A total of ten measurements were taken on the days of the experiment: baseline and after 13 h and 30 min; on the first and second days at 11:00 am (before the physical exercise sessions, during the sessions, and after 3 and 27 h); and on the first and second days at 12:00 pm (immediately after the physical exercise sessions at 50% VO2peak, after 4 and 28 h).

2.4.2. Physical exercise protocol

Ergospirometry was performed using a Quark, PFT (Pulmonary Function Testing device; FRC & DLCO; 4Ergo, Cosmed, Italy). A silicone Hans Rudolph® flow-by-face mask (Kansas City, MO, USA) was employed to improve the comfort of the volunteers. The volunteers were assessed on a treadmill (Life Fitness 9700HR®. Illinois, USA) under normoxia. The participants warmed up for 3 min at 6 km/h and were then subjected to a protocol that consisted of increasing the speed by 1 km/h every minute until voluntary exhaustion. Throughout the test, the treadmill was set to a 1% incline. The variables evaluated in this study were VO2peak and maximum heart rate. The criteria used to determine exhaustion during the ergospirometric test were the inability of the volunteers to maintain the intensity for at least 15 s even when encouraged and a request to stop testing. On the days of the experiment, two sessions of physical exercise were performed, with an intensity of 50% VO2peak for 60 min on a treadmill (Trackmaster®, Maryland, USA) set to a 1% incline. Physical exercise started at 11 am and ended at 12 pm. Volunteers exercised during the 60 min at a speed corresponding to 50% VO2peak.

2.4.3. Polysomnography

All polysomnographies were performed between 10 pm and 7 am. An Embla N7000 polysomnography amplifier with Somnologica Studio version 4 software (Flaga hf, Reykjavik, Iceland) was used to assess sleep patterns. Sleep stages were evaluated according to the criteria described by Iber et al., [24]. The following parameters were assessed: total sleep time (TST) [min], sleep onset latency (min), REM sleep latency (min), sleep efficiency (%), wake after sleep onset (WASO) [min], number of awakenings, sleep stages (N1, N2, N3 and REM sleep) (%), total number of respiratory events, the respiratory disturbance index (RDI) (events/hour), respiratory effort-related arousals (REAs), respiratory events including obstructive, hypopnea central and mixed, the apnea–hypopnea index (AHI, per hour), basal, mean, and minimum oxygen saturation and the number of periodic limb movements (PLM).

The criterion used to identify respiratory events during sleep was based on the American Academy of Sleep Medicine Task Force [25]. Respiratory movements of the chest and abdomen were recorded with calibrated inductance plethysmography sensors, and the oronasal flow was evaluated using a thermistor and a pressure transducer. Oxygen saturation was continuously recorded during the night with a finger pulse oximeter coupled to the polysomnography device. Arousals were defined as abrupt changes in EEG frequency, including the presence of alpha or theta bands, or frequencies above 16 Hz [26].

2.5. Behavioral assessments

Mood and reaction time were assessed under two conditions: pre-and post-exercise. Data were collected by the same psychologist in a bright and quiet room.

2.6. Brunel Mood Scale

This scale was developed to subjectively measure mood [27]. This instrument was adapted from the Profile of Mood States [28] and validated for the Brazilian population by Rohlfis et al. [29]. The scale consists of a list of 24 adjectives associated with the mood state and rates how an individual identifies with each adjective on a 5-point Likert scale where 0 = not at all; 1 = slightly; 2 = moderately; 3 = quite a bit; 4 = extremely. Responses were marked according to the feelings of the volunteers at the time and did not reflect learning. Higher values indicate greater tension, depressed mood, anger, fatigue and confusion, while lower values indicate low vigor. The estimated time of application was 5 min.

3. Vienna Test System

3.1. Simple reaction time

This test evaluates the simple reaction time. The evaluation consists of two visual stimuli (one black circle and one white circle) that constantly appear on the computer screen for short intervals during a 5-min period. The volunteer should respond immediately when the stimuli appear by using their dominant hand to press a black button on the keyboard as soon as possible when the white circle appears on the computer screen. This assessment does not cause learning because the stimuli are random with respect to the order and frequency of appearance. Higher values indicate a longer reaction time [30].

3.2. The Lake Louise scoring system

The Lake Louise scoring system was used to diagnose acute mountain sickness and to assess the severity of symptoms. Based on the Lake Louise consensus criteria, acute mountain sickness is characterized by the presence of headache with at least one other symptom after recent exposure to altitude: gastrointestinal disorders (anorexia, nausea, vomiting), dizziness, insomnia, or fatigue. The diagnosis of acute mountain sickness occurs with a score more than 3 [22]. The estimated time of application was 2 min.

3.3. Statistical analyses

Normality was verified using the Shapiro–Wilk normality test. Data were presented as the mean ± standard deviation (mean ± SD). A repeated measures analysis of variance (ANOVA) followed by Tukey’s post hoc test was used to detect significant differences between groups and times for variables including sleep, mood and reaction time. One-way ANOVA was performed to compare the characteristics of the sample and SaO2% measurements during the day. Statistical analysis was performed using Statistica® version 6, and the level of significance was set at p ≤ 0.05.
4. Results

4.1. SaO₂% during the day and night

The percentage of O₂ saturation was significantly reduced on the second night in HG compared with NG 13 h after the exposure to hypoxia (87.5 ± 0.5 vs. 97.3 ± 0.48; p = 0.0001). The percentage of O₂ saturation was significantly reduced in HG compared with NG on the first and second day, at 3 h (88.1 ± 0.7 vs. 97.6 ± 0.4; p = 0.0001) and 27 h (87.5 ± 0.8 vs. 97.6 ± 0.6; p = 0.0001) after exposure to hypoxia, and during the first and second session of physical exercise at 3.5 h when comparing ENG and NG (95.1 ± 0.8 vs. 97.0 ± 0.1; p = 0.0003; 95.6 ± 0.7 vs. 97.1 ± 0.7; p = 0.0002) or NEG and EHG (85.5 ± 0.9 vs. 95.1 ± 0.8; p = 0.0001; 85.1 ± 0.6 vs. 95.6 ± 0.7; p = 0.0001). The percentage of O₂ saturation was significantly reduced in HG compared with NG on the first and second day immediately after the physical exercise session (87.4 ± 0.5 vs. 97.7 ± 0.4; p = 0.0001) and after 28 h of exposure to hypoxia (88.1 ± 0.3 vs. 97.4 ± 0.4; p = 0.00001). No significant differences were observed in the other groups.

4.2. SaO₂% during sleep

There was a reduction in the percentages of basal O₂ saturation (p = 0.01), mean O₂ saturation (p = 0.006), and minimum O₂ saturation (%) (p = 0.04) in the post-stimulus condition of EHG compared with HG. There was a reduction in the percentages of basal O₂ saturation (p = 0.0001), mean O₂ saturation (p = 0.0001) and minimum O₂ saturation (p = 0.0001) in the post-stimulus condition of HG compared with the pre-stimulus condition in the same group. There was a reduction in the percentages of basal O₂ saturation (p = 0.0001), mean O₂ saturation (p = 0.0001) and minimum O₂ saturation (p = 0.0001) in the post-stimulus condition of EHG compared with the pre-stimulus condition in the same group. There was a reduction in the percentage of basal O₂ saturation (p = 0.0001), mean O₂ saturation (p = 0.0001) and minimum O₂ saturation (p = 0.0001) in the post-stimulus condition.
of HG compared with NG, as shown in Table 3. Fig. 2 provides an example of the sleep stages and O₂ saturation recorded in the arterial blood of four volunteers.

4.3. Physiological sleep variables

Table 2 shows the results for the physiological variables related to sleep. A significant increase in sleep latency (minutes) (p = 0.0007), REM sleep latency (min) (p = 0.02), WASO (min) (p = 0.0004), the number of awakenings (p = 0.0002), stage N1 (%) (p = 0.0001) and stage N2 (%) (p = 0.0004) and a reduction in stage N3 (%) (p = 0.04), REM sleep (%) (p = 0.03), TST (min) (p = 0.04) and sleep efficiency (%) (p = 0.0001) were observed in the post-stimulus condition of HG compared with the pre-stimulus condition in the same group. There was a significant decrease in REM sleep latency (min) (0.0001) and an increase in TST (min) (p = 0.005) and REM sleep (%) (0.0003) in the post-stimulus condition of ENG compared with the pre-stimulus condition in the same group. A significant increase in sleep latency (min) (p = 0.03) was observed in the post-stimulus condition of EHG compared with the pre-stimulus condition in the same group. There was a significant increase in sleep latency (min) (p = 0.0002), REM sleep latency (min) (0.0004), WASO (min) (p = 0.0004), the number of awakenings (p = 0.01), stage N1 (%) (p = 0.0001) and stage N2 (%) (p = 0.005) and a reduction in stage N3 (%) (p = 0.001), REM sleep (%) (p = 0.001), TST (min) (p = 0.01) and sleep efficiency (%) (p = 0.0001) in the post-stimulus condition of HG compared with NG. There was a significant decrease in stage N2 (%) (p = 0.04) and an increase in REM sleep (%) (p = 0.03) in the post-stimulus condition of ENG compared with NG. A significant increase in sleep latency (p = 0.03) and REM sleep (%) (0.0003) were observed in the post-stimulus condition of EHG compared with HG. PLM (per hour) did not differ between the pre- and post-stimulus conditions or between groups.

4.4. Sleep-related respiratory variables

Table 3 shows the results for the sleep-related respiratory variables. There was a significant increase in total respiratory events (p = 0.0001), RDI (n/per hour) (p = 0.0006), central respiratory events (p = 0.0001), hypopnea (p = 0.0002), apnea per hour (p = 0.009), hypopnea per hour (p = 0.002) and AHI (p = 0.009) in the post-stimulus condition of HG compared with the pre-stimulus condition in the same group. There was a significant increase in total respiratory events (p = 0.0006), RDI (n/per hour) (p = 0.003), central respiratory events (p = 0.04), hypopnea (p = 0.001), apnea per hour (p = 0.02), hypopnea per hour (p = 0.007), and AHI (p = 0.02) in the post-stimulus condition of EHG compared with the pre-stimulus condition in the same group. There was a significant increase in total respiratory events (p = 0.0006), RDI (n/per hour) (p = 0.005), central respiratory events (p = 0.0001) hypopnea (p = 0.0006), apnea per hour (p = 0.01), hypopnea per hour (p = 0.009) and AHI (p = 0.03) in the post-stimulus condition of HG compared with NG. The number of RERAs, mixed and obstructive events were not different between the pre- and post-stimulus conditions or between groups.

4.5. Mood

Table 4 shows the results for the mood variables. There were significant impairments in the depressed mood (p = 0.01), anger (p = 0.0001), fatigue (p = 0.0001), tension (p = 0.0003) and vigor (p = 0.007) parameters in the post-stimulus condition of HG compared with the pre-stimulus condition in the same group. Significant impairments in anger (p = 0.002), fatigue (p = 0.004), tension (p = 0.01) and vigor (p = 0.02) were observed in the post-stimulus condition of HG compared with NG. A significant impairment in fatigue (p = 0.03) and improvement in tension (p = 0.02) were observed in the
post-stimulus condition of ENG compared with the pre-stimulus condition in the same group. An improvement of the depressed mood (p = 0.03), anger (p = 0.001), tension (p = 0.0004) and vigor (p = 0.003) parameters were observed in the post-stimulus condition of EHG compared with HG.

4.6. Reaction time

Fig. 3 shows the results for the reaction time variables. A significant impairment in reaction time (p = 0.0001) was observed in the post-stimulus condition of HG compared with the pre-stimulus condition in the same group. A significant improvement in reaction time (p = 0.02) was observed in the post-stimulus condition of EHG compared with the pre-stimulus condition in the same group. A significant impairment in reaction time (p = 0.0001) was observed in the post-stimulus condition of HG compared with that of NG. An improvement in reaction time (p = 0.0001) was observed in the post-stimulus condition of ENG compared with HG. A significant improvement in reaction time (p = 0.0001) was observed in the post-stimulus condition of HG with the pre-stimulus condition in the same group. There was an improvement in the reaction time (p = 0.0001) in the post-stimulus condition in EHG compared with the pre-stimulus condition in HG.

5. Discussion

The present study demonstrated poor sleep efficiency after 13 h under hypoxia, which may have contributed to the impairments in mood and reaction time observed after hypoxic conditions had persisted for 28 h. In contrast, the acute physical exercise performed at 50% VO2peak under hypoxia improved sleep efficiency, wake after sleep onset, stage N3 and REM sleep, which were impaired by hypoxia, and may have contributed to the improvement of mood and reaction time compared with the Hypoxia group but not with respect to normoxia. Studies demonstrate that hyperventilation at altitudes up to 3500 m, SaO2 can be reduced, and the apnea–hypopnea index and central respiratory events can be increased [31,32,33]. Johnson et al.[34], Thakur et al.[31] and de Aquino Lemos et al.[5] showed that altitudes between 3500 and 4500 m can increase the number of awakenings and sleep onset latency, impair the efficiency of sleep, decrease TST and promote changes in sleep architecture, including increases in stages N1 and N2 and reduced slow-wave sleep and REM sleep. These results were confirmed in the present study.

The mechanisms that mediate the deterioration of sleep at higher altitudes have not yet been fully elucidated. However, it might be partially explained by the decreased O2 saturation inspired by the environment, resulting in decreased carbon dioxide (CO2) concentrations in the arterial blood during sleep, which then changes the sleep architecture [35, 36,37]. Accordingly, Rojc et al.[38] reported that hypocapnia induced by hyperventilation during sleep contributes to an increase in respiratory pauses and repeated arousals, which fragment sleep and impair its quality. The respiratory pauses caused by the ventilatory response to hypocapnia increase hypoxemia and consequently stimulate ventilation and awakenings as part of a vicious cycle that then affects sleep [39].

Sleep fragmentation under hypoxia may have contributed to the increase in stages N1 and N2 observed in this study, increasing superficial sleep, which results in less restful sleep and in changes in sleep quality and increase in stage N3.

Table 3
Respiratory pattern of the volunteers during sleep.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Normoxia Mean ± (SD)</th>
<th>Hypoxia Mean ± (SD)</th>
<th>Exercise under normoxia Mean ± (SD)</th>
<th>Exercise under hypoxia Mean ± (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Total respiratory events</td>
<td>15.10 ± (7.24)</td>
<td>14.40 ± (6.29)</td>
<td>19.20 ± (3.85)</td>
<td>19.92 ± (15.02)</td>
</tr>
<tr>
<td>RDI (number/hour)</td>
<td>2.74 ± (1.62)</td>
<td>2.21 ± (1.03)</td>
<td>3.57 ± (1.64)</td>
<td>12.53 ± (3.45)</td>
</tr>
<tr>
<td>RERAs (number)</td>
<td>11.7 ± (7.89)</td>
<td>9.10 ± (4.21)</td>
<td>17.10 ± (11.23)</td>
<td>13.90 ± (9.34)</td>
</tr>
<tr>
<td>Obstructive events</td>
<td>0.80 ± (0.63)</td>
<td>2.30 ± (1.45)</td>
<td>0.40 ± (0.23)</td>
<td>2.90 ± (1.56)</td>
</tr>
<tr>
<td>Hypopnea events</td>
<td>2.40 ± (1.94)</td>
<td>2.80 ± (1.17)</td>
<td>1.40 ± (0.90)</td>
<td>49.40 ± (11.23)</td>
</tr>
<tr>
<td>Central events</td>
<td>0.20 ± (0.10)</td>
<td>0.20 ± (0.05)</td>
<td>0.30 ± (0.48)</td>
<td>25.80 ± (12.89)</td>
</tr>
<tr>
<td>Mixed events</td>
<td>0.03 ± (0.00)</td>
<td>0.00 ± (0.05)</td>
<td>0.00 ± (0.04)</td>
<td>0.00 ± (0.04)</td>
</tr>
<tr>
<td>Apnea (per hour)</td>
<td>0.23 ± (0.17)</td>
<td>0.31 ± (0.23)</td>
<td>0.15 ± (0.10)</td>
<td>0.12 ± (0.24)</td>
</tr>
<tr>
<td>Hypopnea (per hour)</td>
<td>0.36 ± (0.01)</td>
<td>0.46 ± (0.10)</td>
<td>0.43 ± (0.05)</td>
<td>8.90 ± (2.34)</td>
</tr>
<tr>
<td>AHI</td>
<td>0.57 ± (0.14)</td>
<td>0.79 ± (0.09)</td>
<td>0.58 ± (0.16)</td>
<td>12.44 ± (6.45)</td>
</tr>
<tr>
<td>Basal O2 saturation (%)</td>
<td>0.93 ± (0.82)</td>
<td>0.67 ± (0.52)</td>
<td>0.96 ± (0.26)</td>
<td>1.68 ± (0.23)</td>
</tr>
<tr>
<td>Mean O2 saturation (%)</td>
<td>0.95 ± (0.83)</td>
<td>0.96 ± (0.52)</td>
<td>0.78 ± (0.15)</td>
<td>0.85 ± (0.15)</td>
</tr>
<tr>
<td>Minimum O2 saturation (%)</td>
<td>0.92 ± (1.35)</td>
<td>0.91 ± (1.77)</td>
<td>0.91 ± (1.64)</td>
<td>77.40 ± (2.95)</td>
</tr>
</tbody>
</table>

Results are expressed as the mean ± (standard deviation). Sleep-related respiratory variables were compared using repeated measures analysis of variance (ANOVA) followed by Tukey’s post hoc test. The significance level was set at p ≤ 0.05. Acronyms: AHI = apnea-hypopnea index; RDI = respiratory disturbance index; RERAs = respiratory effort-related arousals. a differs from the pre-stimulus condition (normoxia or hypoxia) in the same group; b differs from the post-stimulus condition of the normoxia group; c differs from the post-stimulus condition of the hypoxia group.

Table 4
Mood of the volunteers.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Normoxia Mean ± (SD)</th>
<th>Hypoxia Mean ± (SD)</th>
<th>Exercise under normoxia Mean ± (SD)</th>
<th>Exercise under hypoxia Mean ± (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Tension</td>
<td>2.20 ± (1.00)</td>
<td>1.90 ± (0.90)</td>
<td>1.10 ± (0.70)</td>
<td>5.00 ± (2.30)</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>0.40 ± (0.12)</td>
<td>0.80 ± (0.78)</td>
<td>0.60 ± (0.23)</td>
<td>3.20 ± (1.11)</td>
</tr>
<tr>
<td>Anger</td>
<td>0.70 ± (0.56)</td>
<td>0.80 ± (0.02)</td>
<td>0.80 ± (0.17)</td>
<td>4.90 ± (1.20)</td>
</tr>
<tr>
<td>Vigor</td>
<td>9.40 ± (2.36)</td>
<td>7.50 ± (2.32)</td>
<td>7.90 ± (1.52)</td>
<td>4.50 ± (0.97)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2.10 ± (1.01)</td>
<td>3.30 ± (1.76)</td>
<td>2.10 ± (0.99)</td>
<td>7.50 ± (2.74)</td>
</tr>
<tr>
<td>Confusion</td>
<td>1.10 ± (0.83)</td>
<td>1.80 ± (0.23)</td>
<td>0.30 ± (0.03)</td>
<td>1.70 ± (0.90)</td>
</tr>
</tbody>
</table>

Results are expressed as the mean ± (standard deviation). Mood variables were compared using repeated measures analysis of variance (ANOVA) followed by Tukey’s post hoc test. The significance level was set at p ≤ 0.05. a differs from the pre-stimulus condition (normoxia or hypoxia) in the same group; b differs from the post-stimulus condition of the normoxia group; c differs from the post-stimulus condition of the hypoxia group.
architecture [40,41,42]. As a result, stage N3 and REM sleep were reduced. This reduction may have impaired mood and reaction time because proper physiological and cognitive functions are influenced by slow-wave sleep and REM sleep [43,44,45]. Other parameters, such as sleep onset latency, TST, sleep efficiency, WASO and the number of awakenings, that were altered in our study in the hypoxia group reflect poor sleep quality.

It has been reported that changes in sleep patterns can adversely affect mood and reaction time [46,47,48]. One hypothesis is that the impaired sleep and mood observed in the hypoxia group may have been due to increased concentrations of noradrenaline and dopamine and a reduced concentration of serotonin, which have been observed under these conditions [49]. Changes in the concentration of these neurotransmitters can influence sleep and mood and consequently decrease reaction time [50,51,52].

Different strategies are often employed to minimize the deleterious effects induced by hypoxia, such as the use of O₂ supplements [8], dietary supplements [9,11,53] and administration of pharmacological agents [10,12,13]. In the present study, physical exercise was used as an alternative approach in an attempt to minimize the harmful effects of hypoxia on sleep, mood and cognition.

The practice of physical exercise improves sleep quality [54,55]. However, little is known about the effects of physical exercise on psychobiological aspects and sleep under hypoxic conditions. A recent study performed by Wong Halaki and Chow [56] showed that a single session of aerobic exercise for 60 min at different intensities (55%, 65% or 75% of VO₂peak) improved sleep quality in healthy young individuals. Youngstedt, O’Connor and Dishman [57] and Youngstedt et al. [58] showed that 1 h of acute and moderate physical exercise can maintain good sleep quality by reducing stage N2, sleep onset latency and awakenings. It also increases TST, stage N3 and REM sleep. These results are similar to some extent to those observed in the present study, where an increased percentage of sleep efficiency, stage N3 and REM sleep and reduced awakenings after sleep onset in EHG were observed. These data indicate that physical exercise reduced stage N2 and increased stage N3 and REM sleep in EHG, contributing to deeper and restorative sleep [59]. Furthermore, it is clear that the increased REM sleep observed in ENG was associated with the reduced percentage of stage N2 [60].

Similar to the results of the present study, Kishi et al. [59] reported that physical exercise induces positive effects on dynamic sleep and promotes increases in deeper sleep stages (N3) and decreases in lighter sleep stages (N1 and N2) in healthy people, suggesting increased sleep pressure and improved sleep quality. However, the mechanisms by which physical exercise alters the stage of sleep remains uncertain [59].

The respiratory sleep parameters of EHG were not significantly different, and other mechanisms may therefore have mediated the improvement in sleep. In addition, the mechanisms by which physical exercise improves sleep quality are most likely multifactorial and are still uncertain [61,55]. The most important mechanism by which sleep might be improved with acute physical exercise is the reduction of anxiety because strategies that decrease anxiety may be improving sleep quality [62]. One other factor that may modulate the effects of physical exercise on sleep under hypoxia might be the same as under normoxia, i.e., the hypothesis of body restoration, in which physical exercise generates an energy expenditure greater than the baseline, which is reestablished during sleep, causing sleep to be deeper to N3 stage and restorative [63,64,65]. In addition, it is believed that the effect of physical exercise combined with the effect of hypoxia increases energy expenditure, leading to deeper and restorative sleep, which in turn improves behavioral aspects more effectively, as demonstrated by the improved quality of sleep observed in EHG. These findings are in agreement with Adam and Oswald [66] and McGinty and Szymbusia [67], who demonstrated the beneficial effects of physical exercise on sleep.

Good sleep quality mediated by physical exercise may have directly or indirectly influenced the mood and reaction time parameters. We speculate that the immediate effects of physical exercise on mood and reaction time under hypoxia are due to an increase in metabolism and cerebral blood flow that in turn improves cognitive functions, specifically concerning reaction time and mood, similar to normoxia [68,69,70]. The increase in cerebral blood flow caused by physical exercise may have increased the oxygen supply to the brain and brain-derived neurotrophic factor (BDNF), which are associated with good cognitive functioning and mood [71,72].

6. Conclusion

Our results demonstrate that hypoxia impairs sleep quality and efficiency, reaction time and mood. However, acute, physical exercise at 50% VO₂peak under hypoxia improves sleep efficiency. The mood state and reaction time were improved directly after acute physical exercise was performed. Our results represent the effects of acute exposure to hypoxia and exercise; the effects of chronic exposure to both situations should be investigated in future studies.

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References


