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**Does Exercise Have a Protective Effect on Cognitive Function under Hypoxia? A Systematic Review with Meta-Analysis**

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**Abstract**

**Purpose:** To examine (1) the independent effects of hypoxia on cognitive function and (2) the effects of exercise on cognition while under hypoxia.

**Methods:** Design: Systematic review with meta-analysis. Data sources: PubMed, Scopus, Web of Science, PsychInfo, and Sports Discus were searched. Eligibility Criteria for Selecting Studies:Randomized controlled trials (RCT) and non-randomized controlled studies that investigated the effects of chronic or acute exercise on cognition under hypoxia were considered (Aim 2); or studies investigating the effects of hypoxia on cognition (Aim 1).

**Results:** In total, 18 studies met our inclusionary criteria for the systematic review and 12 studies were meta-analyzed. Exposure to hypoxia impaired attentional ability (SMD = -0.4), executive function (SMD =-0.18), and memory function (SMD = -0.26), but not information processing (SMD = 0.27). Aggregated results indicated that performing exercise under hypoxia setting had a significant effect on cognitive improvement (SMD = 0.3, 95% CI 0.14 to 0.45, *I2* = 54%, *p* < 0.001). Various characteristics (e.g., age, cognitive-task type, exercise type, exercise intensity, training type, and hypoxia level) moderated the effects of hypoxia and exercise on cognitive function.

**Conclusions:** Exercise during exposure to hypoxia improves cognitive function. This association appears to be moderated by individual and exercise/hypoxia-related characteristics.

**Keywords:** cognition; hypoxia; memory; executive function; exercise

**Registration number:** CRD42019145773

1. **Introduction**

Cognitive functions are brain-based skills that allows human to carry out tasks at various levels of difficulty, which are critical in day-to-day life.[1](#_ENREF_1), [2](#_ENREF_2) Notably, cognitive performance is possibly affected by environmental cues such as ambient temperature and altitude.[3](#_ENREF_3), [4](#_ENREF_4) For instance, increasing altitude and the ensuing severity of hypoxia may attenuate the oxygen delivery to the brain tissue. Such, exponentially reduced oxygen fraction during inspiration may result in impairment of brain function and cognitive abilities, including executive function, attention, episodic memory, and information processing.[5-7](#_ENREF_5) This occurrence may be detrimental for particular populations, including those in the armed forces, athletes, mountaineers, mountain rescuers, and other high-altitude residents who are repeatedly exposed to hypoxic conditions.[8-10](#_ENREF_8)

Findings from several primary studies11-12 and a previously published review13 have indicated hypoxia-induced cognitive deficits. Regardless of cognitive task types (i.e., central executive vs. non-executive tasks) and hypoxic conditions (i.e., hypobaric vs normobaric hypoxia), low PaO2 level is strongly associated with greater reductions in cognitive function. In contrast, accumulating evidence suggest that hypoxia has no negative effects on cognitive function.14-17 For instance, an experimental study by [Lefferts, et al.9](#_ENREF_9)showed that response accuracy on cognitive tasks was similar in normoxia compared to hypoxia in a mixed sample of young men and women. [Sun, et al.18](#_ENREF_21) reported that moderate hypoxia did not alter either reaction time or accuracy in sedentary young adults. Given the conflicting findings in previous studies along with new publications on this topic, an updated systematic review is needed to evaluate and synthesize the current evidence on the effects of hypoxia on cognition.

Behavioral approach, such as exercise, has previously been shown to enhance cognitive function and prevent neurocognitive disorders.19-22 Notably, the majority of these previous studies investigating the cognitive benefits of exercise were conducted under normoxic conditions. Recent exploratory studies suggested that moderate exercise has the potential to improve cognitive function during exposure to moderate or severe hypoxia,3, 10, 16, 23 whereas others reported that cognitive function may be impaired if exercise occurred under hypoxic conditions.8, 24 In 2019, a narrative review qualitatively examined the combined effects of exercise and hypoxia on cognitive function, suggesting that these effects are largely determined by the interaction of moderators, such as exercise duration and intensity, hypoxia level and duration, and cognitive-task type.25

Despite this recent narrative review,25 current data investigating the quantitative effects of hypoxia on cognition and whether exercise modifies this effect are inconsistent, which may be due to differences in methodological and experimental conditions. Given the heterogeneity of these aforementioned results, further studies are required to test the moderator effects of experimental conditions on cognitive function in relation to hypoxia and exercise.26, 27 Therefore, to provide a comprehensive review of the extant research on this topic, the current meta-analysis addresses two primary aims. The first aim was to investigate the independent effects of hypoxia on cognitive function. Next, the second aim was to examine the effects of exercise on cognition while under hypoxia. Based on these aims, we further performed subgroup analyses to evaluate potential moderators of the direction and magnitude of the effect sizes. The potential moderators included key study characteristics (e.g., hypoxia protocol, exercise protocol, and specific cognitive task) and participant attributes (e.g., sex, age) were selected because they have been shown to affect cognitive function or influence the effects of exercise on cognitive function while under hypoxia.20, 25

1. **Methods**

**2.1 Protocol and registration**

This study protocol was registered at the PROSPERO and approved with registration number: CRD42019145773.

* 1. **Search strategy**

To obtain adequate and efficient coverage of relevant literature, we used PubMed, Scopus, Web of Science, PsychInfo, and SPORTDiscus for the literature search. All documents were retrieved from inception to August, 2019. Three groups of search terms were combined to locate studies: (1) “exercise” OR “training” OR “sport” OR “physical activity” OR “strength”; (2) “cognition” OR “cognitive function” OR “executive function” OR “cognitive flexibility” OR “cognitive task” OR “neuropsychological test” OR “perception” OR “reaction time” OR “memory” OR “mental” “processing” OR “inhibition”; (3) “hypoxia” OR “hypobaric” OR “normobaric” OR “high altitude”. Reference lists of selected studies will be further investigated to avoid missing any relevant article. We performed this systematic review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guideline.

**2.3 Eligibility criteria**

Firstly, in this review we only included English-language studies published in peer-reviewed journals with obtainable full-text. Secondly, given that this is the first systematic review on this topic, studies that investigated the effects of hypoxia on cognition or experimental studies of randomized controlled trials (RCT) and non-randomized controlled studies (NRS) that investigated the effects of chronic or acute exercise on cognition under hypoxia were considered (Aim 2). Thirdly, sufficient information (e.g., arterial oxygen saturation and/or altitude) were provided so that PaO2 can be estimated. Fourth, at least one cognitive outcome measure of cognition had to be reported, to be extracted for meta-analyses.

* 1. **Collection of studies**

Allrecords from the searched databases were managed with an EndNote library. This literature management toolhelped removed record duplications from different searched databases. Based on the pre-determined eligibility criteria, titles and abstracts of the remaining records were independently screened by two review authors to exclude studies, followed by full-text article assessment. If any disagreement occurred, a third review author was invited to achieve consensus through discussion.

* 1. **Data extraction**

We use a customized form for data extraction. Detailed information included first author of article and publication year, characteristics of participants (sample size and mean age/age range), study design, normoxia/hypoxia protocol, hypoxia-exercise temporality, exercise protocol, the instrument measuring and the reporting of outcome, and statistical analyses and results. To obtain pooled effect size of outcomes, we also extracted quantitative data: (1) mean and standard deviation (SD) of cognitive function between performing tasks under hypoxia and normoxia at rest and its corresponding sample size (Aim 1); (2) mean and SD of cognitive function between performing tasks under hypoxia during exercise and rest and its corresponding sample size (Aim 2); (3) mean and SD of pre-to-post difference, along with sample size of both experimental and control groups.

* 1. **Methodological quality assessment**

Two authors used the modified Downs and Black checklist to independently perform methodological quality assessment of both RCTs and non-RCTs.28 This assessment consists of 24 items across 4 domains (reporting, external validity, internal validity, and power) and scoring ranged from zero to 25, with higher scores representing better methodological quality.

* 1. **Classification of study aims**

The study was classified as two specific aims regarding the association between hypoxia and exercise on cognitive function. The first specific aim was to explore the effects of hypoxia on cognitive function. The first aim compared cognitive performance between two groups, with one group performing the cognitive task during exposure to hypoxia and the other group completing the cognitive task during normoxia. Next, the second specific aim was to examine the effects of exercise on cognitive function while under hypoxia. The second aim compared cognitive performance between two groups, with one group performing the cognitive task and exercise under a hypoxic condition, with the other group completing the cognitive task under hypoxia (no exercise).

* 1. **Statistical analysis**

The comprehensive Meta-Analysis software (Version 3, Biostat, NJ, USA) was used to calculate effect sizes (standardized mean difference, SMD) representing the magnitude of the exercise intervention on cognition. SMD is considered as small (0.2-0.49), moderate (0.5-0.79) and large (≥ 0.8). Considering that the outcomes and unit of cognitive measures vary across the selected studies, the random-effects model was used along with 95% confidence interval (CI). We use I-squared to check heterogeneity, with 25%, 50%, and 75% that reflect small, medium, and large heterogeneity, respectively. Publication bias was assessed by Egger’s test along with a visually presented funnel plot.

The ESs (effect sizes) heterogeneity was assessed by *Q* statistics. *Q* statistics evaluate the null hypothesis that all individual ESs compute the same population ES. Statistically significant *Q* statistics indicate the existence of possible moderator variables.29 The moderator analyses were conducted to test if the above-mentioned moderators influenced the overall ESs.20, 25 Meta-regression was used for continuous variables (hypoxia duration, hypoxia level, and hypoxia dose [multiplied hypoxia duration by hypoxia level], and exercise duration) to quantify the relationship between the magnitude of the moderator and cognitive function,30 while subgroup-analyses were performed based on categorical variables, including sex, age (young adults = 20-24 years vs. older adults = 60 years and above), study design (RCT or non-RCT), cognitive-task type, exercise type, exercise intensity, exercise temporality, training type, and cognitive-task type. We computed a mean ES and standard error for each group, and then tested whether these mean ESs are significantly different from one another, which model is analogous to a one-way random effects ANOVA model.31

1. **RESULTS**

Fig. 1 displays the flow chart of the literature search process. The computerized searches yielded 527 articles. Among the 527 articles, 161 were eliminated due to duplication and 363 articles were screened. After initial screening of 363 titles and abstracts, 26 full text articles were reviewed. Among these 26 articles, 8 were ineligible as they did not meet the inclusion criteria or did not provide sufficient data to calculate ESs. Therefore, in total, 18 studies met our inclusion criteria for the systematic review and 12 studies were eligible for the quantitative meta-analysis.

* 1. **Study characteristics**

Detailed information on study characteristics is displayed in Table 1. Sample size across included studies ranged from 8 to 80 participants, with mean age varying from 20 and 92 years old.[32](#_ENREF_32), [33](#_ENREF_33) Among the 18 studies, 6 (33%) were RCT and 12 (67%) were NRS. The hypoxia protocol varied, including, for example, hypoxia duration (e.g., ranging from 5-min to 180-min), hypoxia level (e.g., ranging from FIO2 10% to 18%), and hypoxia dose (e.g., ranging from 0.73 to 25.38). The exercise protocol varied by exercise type (e.g., cycle ergometer, a full body strength-endurance program, multimodal training program, and repeated sprint running), exercise intensity (e.g., light, moderate, and high), exercise duration (e.g., ranging from 5-min to 165-min), exercise temporality (e.g., exercise occurred during hypoxia, or both before and during hypoxia) and training type (e.g., acute exercise [also referred to as a single bout of exercise] and chronic exercise [also referred to as a training]). Cognitive tasks were categorized into information processing, attention-based ability, executive function, memory, and reaction time, and all information are presented in the Table 2. Of the 18 studies, 12 (67%) employed acute exercise interventions and 6 (33%) employed chronic exercise interventions.

* 1. **Study quality**

Based on the modified Downs and Black checklist, the methodological quality of the included studies was robust (21.31 ± 1.49: mean ± SD), ranging from 19 to 24, considering the total maximum score of 25. All studies were within 3 SD of the mean scores and, thus, were included in the meta-analysis.[34](#_ENREF_34)

* 1. **Reasons of exclusion for each study screened by full text**

Detailed reasons of exclusion for each study, of which full text was screened, were extracted and are presented in Table 3. Examples included history of chronic diseases and physical problems during exercise or hypoxia, experience of smoking, medication use, or cognitive disorders, exposure to hypoxia or high altitude within several months prior to the study, and engagement in regular exercise training prior to the study.

* 1. **Meta-analysis of effects on cognitive outcomes**

Among these 12 studies, 31 ESs examining the effect of hypoxia on cognition were calculated. As illustrated by Fig. 2 (Aim 1), aggregated results indicated a non-statistically significant association between the presence of hypoxia and an overall lower cognition (SMD = -0.13, 95% CI -0.28 to 0.01, *I2* = 45%, *p* = 0.075).

Among these 12 studies, 29 ESs examining the effect of exercise on cognition under hypoxia were calculated. As illustrated by Fig 3 (Aim 2), the aggregated results indicated that performing exercise under a hypoxia setting has significant effects on cognitive improvement (SMD = 0.3, 95% CI 0.14 to 0.45, *I2*= 54%, *p* < 0.001).

* 1. **Moderator analyses**

For Aim 1, in the sub-group analyses (Table 4), the effect of hypoxia on cognition was significantly moderated by sex (Qb = 15.22, *df* = 2, *p* < 0.001) and cognitive task type (Qb = 10.33, *df* = 3, *p* = 0.016), but not by other variables. Furthermore, males (SMD = -0.3, 95% CI -0.48 to -0.11) suffered significant cognitive impairment when being exposed to hypoxia, as compared with females (SMD = 0.39, 95% CI 0.09 to 0.69) and mixed sexes (SMD = 0.02, 95% CI -0.19 to 0.22). Exposure to hypoxia impaired attentional ability (SMD = -0.4, 95% CI -0.88 to 0.09), executive function (SMD = -0.18, 95% CI -0.39 to 0.02), and memory function (SMD = -0.26, 95% CI -0.55 to 0.04), but improved information processing (SMD = 0.27, 95% CI 0.00 to 0.53). In the meta-regressions, the hypoxia-cognition associations did not differ by these hypoxia characteristics (hypoxia duration [Z = 1.32, 95% CI 0.00 to 0.00, *p* = 0.19], hypoxia level [Z = -0.80, 95% CI -0.11 to 0.05, *p* = 0.42], and hypoxia dose [Z = 1.16, 95% CI 0.00 to 0.03, *p* = 0.25]), which is displayed in the Supplementary Fig 4.

For Aim 2, in the sub-group analyses (Table 5), the effect of exercise under hypoxia on cognition was significantly moderated by age (Qb = 6.30, *df* = 1, *p* = 0.012), cognitive-task type (Qb = 9.34, *df* = 3, *p* = 0.025), exercise type (Qb = 17.12, *df* = 3, *p* = 0.001), exercise intensity (Qb = 3.98, *df* = 1, *p* = 0.046), and training type (Qb = 6.30, *df* = 1, *p* = 0.012). Furthermore, older adults (SMD = 0.51, 95% CI 0.32 to 0.69) benefited more from exercise under hypoxia than those young adults (SMD = 0.16, 95% CI -0.04 to 0.36). Exercising under hypoxia had the greatest (favorable) impact on attention (SMD = 0.78, 95% CI 0.39 to 1.17) compared to information processing (SMD = 0.26, 95% CI 0.03 to 0.49), executive function (SMD = 0.07, 95% CI -0.19 to 0.33), and memory (SMD = 0.38, 95% CI 0.12 to 0.64). Full body strength-endurance programs (SMD = 0.70, 95% CI 0.39 to 1.01) were more effective than cycle ergometer (SMD = 0.23, 95% CI 0.06 to 0.40), multimodal training program (SMD = 0.50, 95% CI 0.14 to 0.85), and repeated sprint running (SMD = -0.71, 95% CI -1.38 to -0.04) in improving cognitive function. Exercising at moderate intensity (SMD = 0.36, 95% CI 0.22 to 0.50) had greater effects on cognitive improvement when compared to high intensity exercise (SMD = -0.41, 95% CI -1.16 to 0.34). Chronic exercise (SMD = 0.51, 95% CI 0.32 to 0.69) was more effective than acute exercise (SMD = 0.16, 95% CI -0.04 to 0.36) in enhancing cognitive function. In the meta-regressions, while no significant moderator effect was present for exercise duration (Z = 0.81, 95% CI 0.00 to 0.00, *p* = 0.42), hypoxia duration (Z = 0.42, 95% CI 0.00 to 0.00, *p* = 0.68), and hypoxia dose (Z = 0.05, 95% CI -0.02 to 0.02, *p* = 0.96), there was evidence of moderation effect for hypoxia level (Z = -3.82, 95% CI -0.19 to -0.06, *p* < 0.001), indicating that exercising while at greater hypoxia level was negatively associated with cognitive performance. Results of meta-regression are presented in the Fig 5.

* 1. **Publication bias**

Based on the funnel plot, the Egger’s test of regression intercept was not statistically significant in Aim 1 (intercept = -0.22, *p* = 0.87) and Aim 2 (intercept = -3.37, *p* = 0.13), indicating that there was no evidence of risk of bias across studies.

1. **DISCUSSION**
   1. **Main study findings**

This review included both RCTs and NRSs with consideration of multiple potential moderating variables to systematically evaluate: (1) the effects of hypoxia on cognitive function; (2) the effects of exercise under hypoxia on cognitive function. Firstly, we found that hypoxia exposure impaired some but not all aspects of cognitive function. The effect of hypoxia on cognition was moderated by sex and cognitive task type. Secondly, exercising under hypoxia may have small to medium positive effects on selected aspects of cognitive function. When being exposed to hypoxia, exercise-cognition association was moderated by age, cognitive-task type, exercise type, exercise intensity, training type, and hypoxia level.

* 1. **Comparisons with previous reviews**

As indicated in recent narrative and meta-analytic reviews, cognitive function may be compromised during exposure to hypoxia.13 In alignment with these previous reviews, our meta-analysis demonstrates that hypoxia had a selective effect on cognition, in that hypoxia enhanced information processing, but impaired cognition-based attention, executive function and memory. Even though this result supports the conclusions of other related studies, the magnitude of effect is smaller than previous work. Notably, Taylor et al. reported that hypoxia was more negatively associated with central executive tasks compared with non-executive tasks.11 This, however, is in contrast to the review by McMorris et al. which suggested that there are no significant hypoxia-induced differences between executive- and non-executive tasks.13 Moreover, while the meta-analytic review by McMorris et al. was for within group studies, our work utilized both within and between group studies. These conflicting findings across the literature render challenges in the interpretation of our observations regarding Aim 1. If our findings are replicated and prove to be reliable effects, then future research should aim to evaluate the underlying reasons as to why hypoxia may have a unique effect on selective cognitions. Next, our main findings (Aim 2) demonstrate that exercise under hypoxia had a positive effect on cognitive function, which extends a recently published narrative review on this topic.25

* 1. **Possible explanation for study findings**

Among Aim 1, notably, we found a significant sex-specific effect. That is, performing cognitive task under hypoxia was advantageous in improving cognitive function for females. This may, in part, be attributed to females having relatively higher SpO2 and estrogen hormones than males, which provide a greater resistance to hypoxia.[35-38](#_ENREF_35) However, this neuroprotective effect of estrogen in response to hypoxia should be interpreted with caution as few studies that investigated the hypoxia-cognition interaction for women during a specific timing of the menstrual cycles were included in this review. We also observed significant differences between cognitive-task types. That is, hypoxia had a favorable effect on information processing, as opposed to the observed impairment effect on attention, executive function and memory. Such selected aspects of cognitive impairment are supported by a previous review suggesting that arterial partial pressure of oxygen(PaO2) is a strong predictor of reduced cognitive performance. If PaO2 level is low (35-60mmHg), increased cerebral blood flow may not adequately compensate for the lack of oxygen required to maintain cognitive ability. [Ochi, et al.39](#_ENREF_39)indicated that peripheral oxygen saturation (SpO2) gradually decreases as the severity of hypoxia increases, and low levels of SpO2 may induce cerebral deoxygenation. Hence, it is plausible that hypoxia may be responsible for negative cognitive-related outcomes due to neurological and structural alterations of the brain tissue.40

Regarding Aim 2, we observed moderation effects for age, cognitive task type, exercise type and intensity, and hypoxia level. It is challenging to explain the moderation effects of age. If hypoxia has a greater negative effect on cognition for older adults (vs. younger adults), it is conceivable that exercise may help attenuate this effect in older adults. However, for our Aim 1, we did not observe an age moderation effect. Our findings also demonstrate that attention tends to be more positively influenced by exercise during exposure to hypoxia than other cognitive task types (e.g., information processing, executive function, and memory). Notably, however, all cognitions were enhanced with exercise. Although Chang et al.20 observed that acute exercise under normoxia helped to improve executive function, there are few studies on which types of cognitions are most sensitive to exercise in hypoxic conditions. As such, this is an area in need of future research.

In addition, a notable finding was that full body strength-endurance exercise had a greater impact on cognition improvement. This finding may be related to the cognitive enhancement effects from complex movement patterns, which we have detailed elsewhere.41 Encouragingly, it is anticipated that more complicated movement patterns stimulate regional cerebral flow and cortical excitability, resulting in enhancing cognitive function;42-44 thus, full body strength-endurance exercise, consisting of aerobic exercise and strength training, may aid to exert cognitive ability under hypoxia. Further, we detected a significant difference in effect size for exercise intensity (moderate vs. high). Our findings indicated that moderate-intensity exercise under hypoxia increases cognitive function. This improvement effect is consistent with the moderation results from several previous studies.17, 18, 45 Importantly, however, under normoxia, exercise intensity may differentially influence cognition-based reaction time and accuracy.46 Future work should evaluate this under hypoxic conditions. However, when exposed to hypoxia, moderate-intensity exercise may increase cerebral blood flow and compensate for a decreased SpO2.47, 48 Indeed, exercising under moderate hypoxia favored cognitive benefits when compared to severe hypoxia. Although speculative, this effect may be a result of the potential additive effects of exercise and moderate hypoxia on cognition. As fully discussed elsewhere,18, 49 moderate levels of hypoxia and exercise may enhance synaptic plasticity via an increase expression of brain-derived neurotrophic factor (BDNF). The hypoxia- and exercise-induced upregulation of BDNF can facilitate cerebral neural activation and neurogenesis, and therefore, lead to cognition improvements.50 Lastly, chronic exercise had a more positive effect on cognition than acute exercise under hypoxia. This finding is consistent with previous work demonstrating that acute exercise under normoxia were not as beneficial in enhancing cognitive function when compared to chronic exercise.51 This may be partially attributed to chronic exercise-induced adaptations of physiological and neurological parameters.22, 52, 53 To provide definitive conclusions, longitudinal studies of exercise-training effects on cognition while under hypoxia are needed, as there are limited studies comparing how the length of training intervention affects cognition at different levels of hypoxia.

* 1. **Strengths and limitations**

This meta-analytic review has several strengths. Firstly, this is the first meta-analytic review which has investigated the combined effects of exercise and hypoxia on cognitive function. Secondly, we simultaneously demonstrated the independent effects of hypoxia on cognitive function and the interactive effects of exercise and hypoxia on cognitive function. Lastly, we tested a variety of moderating variables to determine the cause of heterogeneity, which provides a much clearer picture regarding the effects of exercise under hypoxia on cognitive function. Despite these strengths, there are several limitations of our study. Firstly, several moderator effects should be interpreted with caution as small cell sizes in this review evaluated the relationship between exercise and cognition under hypoxia. Although there is limited cell sizes for moderators, the identification of potential moderators will help future work to demonstrate the complexity of these interactions. Secondly, timing of cognitive task in reference to exercise (e.g., before, during, or after exercise) was not considered, and thus, future studies should establish whether different cognitive assessment periods alter our observations. Thirdly, training periods (e.g., short, medium, and long) should be included in further studies to determine the optimal training length for cognition improvement under hypoxia. Moreover, physiological parameters should be investigated to evaluate the underlying mechanisms of our observed effects. Lastly, although meta-analyses provides a rational way to summarize and quantitatively synthesize a large number of previous empirical studies, it is challenging to account for the unique design characteristics of individual experiments.54, 55 Therefore, the results may be biased by systematic confounding factors that correlate with effect size. For example, this problem may be applied to moderation analyses that include small numbers of studies and to between-study comparisons when we are actually interested in within-subject correlations.56, 57

1. **CONCLUSION**

In conclusion, this meta-analysis demonstrates two important findings. Firstly, cognitive function is impaired during hypoxia in resting conditions, particularly for executive function and memory. Second, exercise during exposure to hypoxia plays a key role in improving cognitive function. Various characteristics (e.g., exercise modality) are likely to moderate the relationship between exercise and cognition under hypoxia.

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**Authors’ contributions**

LZ and PL were responsible for conception and design; MJ, JY, SR, PL and LZ conducted the article screenings; MJ, SR and JY extracted data; MJ, MK, PL and LZ performed data analyses and interpretation of results; MJ, PL, ZK, LY, SL, HL, JL and LZ drafted this manuscript; all authors revised this manuscript and agreed with submission.

**Competing interests**

The authors declare that they have no competing interests.

**Figure captions**

Fig.1. Flow chart of literature search.

Fig.2. Forest plot depicting the standardized mean difference effect sizes (hypoxia vs. normoxia) and 95% confidence interval for Aim 1.

Fig.3. Forest plot depicting the standardized mean difference effect sizes (exercise vs. no exercise) and 95% confidence interval for Aim 2.

Fig.4. Effect sizes by moderator variables in meta-regression for Aim 1 (A. Regression of hypoxia duration on SMD; B. Regression of hypoxia level (FIO2) on SMD; C. Regression of hypoxia dose on SMD).

Fig.5. Effect sizes by moderator variables in meta-regression for Aim 2 (A. Regression of exercise duration on SMD; b. Regression of hypoxia duration on SMD; c. Regression of hypoxia level (FIO2) on SMD; d. Regression of hypoxia dose on SMD).

**Tables**

Table 1

Extraction table of the evaluated studies.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Subject**  **Characteristics** | **Study Design** | **Normoxia / Hypoxia Protocol** | **Hypoxia-Exercise Temporality** | **Exercise Protocol** | **Cognitive Function Assessment** | **Results** |
| [Ando, et al.3](#_ENREF_3) | 12 adult males  Mage = 22.9,  SD = 1.5 | Within-subject,  Pre-post comparison | Performed cognitive tasks under either normoxia (20.9%) or normobaric hypoxia (18%, 15%)  / 25-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 5-min of cycle ergometer exercise at 20% peak VO2max and 10-min of cycle ergometer exercise at 60% peak VO2max / Acute exercise | GNG (Go / No-Go) task | <GNG - RT (Reaction Time)>  Main effect EX: *F* (1,11) = 18.73, *p* < 0.01  Main effect HY: *F* (2,22) = 0.06, *p* = 0.94  EX \* HY: *F* (1.41,15.53) = 0.06, *p* = 0.69  <GNG - Accuracy>  Main effect EX: *F* (1,11) = 1.49, *p* = 0.25  Main effect HY: *F* (2,22) = 2.14, *p* = 0.14  EX \* HY: N/A |
| [Schega, et al.32](#_ENREF_32) | 34 retired older adults  (60-70 years) | Between-subject,  Randomized controlled trial (RCT),  Pre-post comparison | The control group (CG) was supplied with a placebo air mixture and the experimental group (EG) was supplied with an IHT (Intermittent Hypoxia Training).  / 10-min of hypoxia (10%) | Hypoxia/Normoxia During Exercise | a full-body strength-endurance exercise program at 50% of maximum force  / Chronic exercise | d2 test:  GZ, SKL  &  ZVT  (Zahlen Verbindungs Test) | <GZ>  Main effect of EX: *F* (1,32) = 36.325, *p* = .00; η² = 0.532  Main effect HY: *F* (1,32) = 0.08, *p* = 0.78; η² = 0.002  EX \* HY: *F* (1,32) = 4.59, *p* = 0.04; η² = 0.125  <SKL>  Main effect EX: *F* (1,32) = 23.565, *p* = .00; η² = 0.424  Main effect HY: *F* (1,32) = 0.047, *p* = 0.831; η² = 0.001  EX \* HY: *F* (1, 32) = 4.65, *p* = 0.034; η² = 0.127  <ZVT>  Main effect EX: *F* (1,32) = 32.065, *p* = .00; η²= 0.501  Main effect HY: *F* (1,32) = 1.906, *p* = 0.177; η² = 0.056  EX \* HY: *F* (1,32) = 0.21, *p* = 0.649; η² = 0.007 |
| [Kim, et al.8](#_ENREF_8) | 8 healthy adult males  Mage = 41,  SD = 2 | Within-subject,  counterbalanced,  Pre-post comparison | In one of the experimental trials (HY, 12.5%), subjects remained resting in a seated position the entire 5 h; in the other experimental trial (HY + EX), subjects rested 2 h, cycled for 1 h, then rested the last 2 h. | Hypoxia/Normoxia both Before and During Exercise | 1 h of a Lode cycle exercise (workload equivalent to 50% altitude adjusted VO2max)  / Acute exercise | Trail Making Test  A and B | Main effect Ex: N/A  Main effect HY: N/A  Ex \* HY: N/A |
| Komiyama, et al.16 | 16 adult males  Mage = 23,  SD = 2.3 | Within-subject,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under normoxic and hypoxic conditions (15%)  / 45-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 30-min of cycle ergometer exercise until heart rate 140 beats/min  / Acute exercise | Spatial DR  (Spatial Delayed Response), GNG task | <Spatial DR - Accuracy>  Main effect EX: *F* (2, 30) = 1.34, *p* = 0.28, η² = 0.08  Main effect HY: *F* (1,15) = 0.81, *p* = 0.38, η² = 0.05  EX \* HY: *F* (2, 30) = 1.69, *p* = 0.20, η² = 0.10  <GNG - Accuracy>  Main effect EX: *F* (2, 30) = 2.79, *p* = 0.08, η² = 0.16  Main effect HY: *F* (1,15) = 2.5, *p* = 0.14, η² = 0.14  EX \* HY: *F* (2, 30) = 1.13, *p* = 0.34, η² = 0.07  <GNG - RT>  Main effect EX: *F* (2, 30) = 8.02, *p* < 0.01, η² = 0.35  Main effect HY: *F* (1,15) = 0.63, *p* = 0.44, η² = 0.04  EX \* HY: *F* (2, 30) = 0.10, *p* = 0.91, η² = 0.006 |
| Seo, et al.45 | 16 young  healthy men  Mage = 24,  SD = 4 | Within-subject, counterbalanced,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under normoxic and hypoxic conditions (12.5%)  / 90-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | Two 15-min bouts of cycle ergometer exercise at 40% and 60% of adjusted VO2max with 15-min recovery period between bouts  / Acute exercise | GNG task, RMCPT  (Running Memory Continuous Performance Task) | <GNG - RT>  Main effect EX: N/A  Main effect HY: *F* = 1.8, *p* = 0.168  EX \* HY: N/A  <GNG - Accuracy>  Main effect EX: N/A  Main effect HY: *F* = 2.2, *p* = 0.098  EX \* HY: N/A  <RMCPT - RT>  Main effect EX: 40% (*p* = 0.028), 60% ( *p* = 0.009)  Main effect HY: *F* = 3.4, *p* = 0.025  EX \* HY: N/A  <RMCPT - Accuracy>  Main effect EX: *p* > 0.262  Main effect HY: *F* = 7.6, *p* ≤ 0.001  EX \* HY: N/A  <RMCPT - Throughout score>  Main effect EX: 40% (*p* = 0.023), 60% ( *p* = 0.006)  Main effect HY: *F* = 5.0, *p* = 0.005  EX \* HY: N/A |
| Dobashi, et al.24 | 8 healthy males  Mage = 23.7,  SD = 2.1 | Within-subject,  counterbalanced,  Pre-post comparison | Performed cognitive tasks before, during, and 60-min after exercise under normoxic and hypoxic conditions (14.1%)  / 180-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | Four 30-min bouts of cycle ergometer exercise at moderate intensity with a 15-min interval rest between each set  / Acute exercise | CWST (Color-Word Stroop Task):  Task 1  (reverse-Stroop control)  Task 2  (reverse-Stroop interference)  Task 3  (Stroop control)  Task 4  (Stroop interference) | <Task 1 - Number of Achievement>  Main effect EX: N/A  Main effect HY: N/A  EX \* HY: *F* (3, 21) = 4.53, *p* < 0.05, η² = 0.39  <Task 3 - Number of Achievement>  Main effect EX: *F* (3, 14) = 4.09, *p* < 0.05, η² = 0.37  Main effect HY: *F* (3,21) = 0.24, *p* > 0.05, η² = 0.03  EX \* HY: *F* (3, 21) = 2.97, *p* > 0.05, η² = 0.30  <Task 2, 4 - Number of Achievement>  Main effect EX: *p* > 0.05  Main effect HY: *p* > 0.05  EX \* HY: *p* > 0.05  <Task 1 - Number of Correct Response>  Main effect EX: N/A  Main effect HY: N/A  EX \* HY: *F* (2, 14) = 5.63, *p* < 0.05, η² = 0.45  <Task 3 - Number of Correct Response>  Main effect EX: *F* (2, 14) = 3.2, *p* > 0.05, η² = 0.31  Main effect HY: *F* (1, 8) = 9.1, *p* < 0.05, η² = 0.57  EX \* HY: *F* (2, 14) = 1.77, *p* > 0.05, η² = 0.20  <Task 2, 4 - Number of Correct Response>  Main effect EX: *p* > 0.05  Main effect HY: *p* > 0.05  EX \* HY: *p* > 0.05 |
| [Lefferts, et al. 9](#_ENREF_9) | 30 adults  M = 15, Mage = 22, SD = 4  W = 15, Mage = 20, SD = 3 | Within-subject,  Pre-post comparison | Performed cognitive tasks during exercise under normoxic and hypoxic conditions (12.5%)  / 120-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 25-min bouts of cycle ergometer exercise at moderate intensity  / Acute exercise | Memory recognition,  N-Back, Flanker tasks | Main effect EX: N/A  Main effect HY: N/A  EX \* HY: N/A |
| [Schega, et al. 33](#_ENREF_33) | 33 older adults  (60-75 years) | Between-subject,  RCT,  Pre-post comparison | The CG breathed ambient air and the EG was supplied with IHT (10%).  / 120-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 30-min bouts of bicycle ergometer at moderate intensity  / Chronic exercise | Stroop Test | <Color task>  Main effect EX: N/A  Main effect HY: *p* = 0.004  EX \* HY: *F* (1,31) = 1.833, *p* = 0.178, η² = 0.056  <Word-color-tasks>  Main effect EX: N/A  Main effect HY: *p* = 0.005  EX \* HY: *F* (1,30) = 1.506, *p* = 0.23, η² = 0.048 |
| Bayer, et al.58 | 34 older adults  (64-92 year) | Between-subject,  RCT,  Pre-post comparison | EG received multimodal training programs (MTP) and internal hypoxic–hyperoxic training (IHHT, 12%). CG received MTP during the IHHT. Both performed cognitive tasks before and after the training. / 35-45 min of hypoxia | Hypoxia/Normoxia During Exercise | 2 h of MTP  (2-3 times per week, 14-15 trainings in 5-6 weeks)  / Chronic exercise | DemTect (Dementia detection test), CDT (Clock-drawing test) | <DemTect>  Main effect EX: + 16.7% vs. -0.39%, *p* < 0.001  Main effect HY: N/A  EX \* HY: N/A  <CDT>  Main effect EX: +10.7% vs. -8%, *p* = 0.031  Main effect HY: N/A  EX \* HY: N/A |
| Bayer, et al.59 | 34 older adults  (64-92 years) | Between-subject,  RCT,  Pre-post comparison | EG received MTP and IHHT (10-14%), and CG received MTP during the simulation of IHHT. Both performed cognitive tasks before and after the training.  / 30-40 min of hypoxia | Hypoxia/Normoxia During Exercise | 2 h of MTP  (2-3 times per week, 12-15 trainings in 5-7 weeks)  / Chronic exercise | DemTect, CDT | <DemTect>  Main effect EX: + 16.7% vs. -0.39%, *p* < 0.001  Main effect HY: N/A  EX \* HY: N/A  <CDT>  Main effect EX: +10.7% vs. -8%, *p* = 0.031  Main effect HY: N/A  EX \* HY: N/A |
| Komiyama, et al.23 | 13 adult males  Mage = 21.5 | Within-subject,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under either normoxic or hypoxic conditions (13%)  / 30-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 20-min of cycle ergometer exercise at moderate intensity  / Acute exercise | Spatial DR,  GNG task | <GNG - RT>  Main effect EX: *F* (1, 12) = 29.52, *p* < 0.001  Main effect HY: *F* (1,12) = 0.16, *p* = 0.69  EX \* HY: N/A  <GNG -Accuracy>  Main effect EX: *p* > 0.14  Main effect HY: *p* > 0.14  EX \* HY: N/A  <Spatial DR – Accuracy>  Main effect EX: *p* > 0.14  Main effect HY: *p* > 0.14  EX \* HY: N/A |
| [Seo, et al.10](#_ENREF_10) | 15 healthy women  Mage = 22,  SD = 2 | Within-subject, counterbalanced,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under either normoxia or hypoxia (12.5%)  / 105-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | Two 15-min of cycle ergometer exercise at 40% and 60% Vo2max with a 15-min recovery between bouts  / Acute exercise | RMCPT | Main effect EX: *F* (4, 56) = 2.6, *p* = 0.047, η²p = 0.2  Main effect HY: N/A  EX \* HY: N/A |
| Stavres, et al.60 | 18 adults  M = 9, Mage = 22, SD= 3  W = 9,Mage = 23, SD=2 | Within-subject, counterbalanced,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under normoxic and hypoxic conditions (12.5%)  / 100-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 20-min of cycle ergometer exercise at moderate intensity  / Acute exercise | MATH (Mathematical performance), RMCPT | <MATH>  Main effect EX: *F*(6, 102) = 3.67, *p* = 0.002  Main effect HY: N/A  EX \* HY: N/A  <RMCPT>  Main effect EX: *F*(6, 102) = 9.64, *p* < 0.001  Main effect HY: N/A  EX \* HY: N/A |
| Limmer, et al61 | 80 adults  Men: 51,  Mage = 25.5, SD= 6  Female: 29,  Mage = 24.8, SD=5.9 | Between-subject,  Pre-post comparison | Group A: HYP + EX (n=15)  Group B: HYP (n=25)  Group C: EX (n=19)  Group D: NOR (n=21) | Hypoxia/Normoxia During Exercise | Group A: Mountain climbing  (7 days)  Group B: Rest in a hypoxic state  Group C: Ski hiking (7 days)  Group D: Rest in a normoxic state / Chronic exercise | Frankfurt Attention Inventory – 2 | <FAIR-2>  Main effect EX: N/A  Main effect HY: N/A  EX \* HY: N/A |
| Bayer, et al.62 | 34 older adults  (64-92 years) | Between-subject,  RCT,  Pre-post comparison | EG received MTP and IHHT (10-14%), and CG received MTP during the simulation of IHHT. Both performed cognitive tasks before and after the training.  / 30-40 min of hypoxia | Hypoxia/Normoxia During Exercise | 30-min of MTP  (2-3 times per week, 12-15 trainings in 5-7 weeks)  / Chronic exercise | DemTect, CDT | Main effect EX: N/A  Main effect HY: N/A  EX \* HY: N/A |
| Lei, et al.17 | 30 healthy inactive women  Mage = 22.6, SD=3.2 | Within-subject,  counterbalanced,  Pre-post comparison | Performed cognitive tasks at rest and during exercise under normoxic and hypoxic conditions (12%)  / 20-min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 10-min bouts of cycle ergometer exercise at moderate intensity  / Acute exercise | Interference control task | <Interference control task – RT>  Main effect EX: *F* (1,29) = 8.336, *p* = 0.011, η²p = 0.203  Main effect HY: F(1,29) = 5.425, p = 0.043, η²p = 0.134  EX \* HY: *F* (1,29) = 0.524, *p* = 0.573, η²p = 0.011  < Interference control task – Accuracy>  Main effect EX: *F* (1,29) = 0.487, *p* = 0.445, η²p = 0.02  Main effect HY: *F* (1,29) = 0.777, *p* = 0.796, η²p = 0.002  EX \* HY: *F* (1,29) = 0.03, *p* = 0.798, η²p = 0.002 |
| Morrison, et al.63 | 11 amateur team-sport athletes  Mage = 22.8, SD=3.6 | Within-subject,  counterbalanced,  Pre-post comparison | Performed cognitive tasks before and after exercise under normoxic and hypoxic conditions (14.5%)  / 5-min of hypoxia | Hypoxia/Normoxia During Exercise | A repeated-sprint running protocol  (4 sets of 4, 4-s all-out sprints)  / Acute exercise | DET  (Detection task)  IDN  (Identification task)  OCL  (One card learning task ) | <DET>  Main effect EX: N/A  Main effect HY: N/A  EX \* HY: N/A  <IDN>  Main effect EX: N/A  Main effect HY: N/A  EX \* HY: N/A  <OCL - RT>  Main effect EX: *F* = 10.62, *p* = 0.01, η² = 0.52  Main effect HY: *F* = 0.3, *p* = 0.56, η² = 0.03  EX \* HY: *F* = 0.29, *p* = 0.60, η² = 0.03  <OCL – Accuracy>  Main effect EX: N/A  Main effect HY: *p* = 0.20  EX \* HY: N/A |
| Sun, et al.18 | 20 inactive adults  (M: 10, W:10)  Mage = 23.9, SD=2.5 | Between-subject,  RCT,  Pre-post comparison | Performed cognitive tasks before and after exercise under normoxia and hypoxia (15.4%) / 30-40 min of hypoxia | Hypoxia/Normoxia both Before and During Exercise | 6-mins of cycle ergometer exercise at high intensity  (10 repetitions of 6 s with 30 s of recovery)  / Acute exercise | GNG task | <GNG - RT>  Main effect EX: *p* = 0.204, η² = 0.083  Main effect HY: *p* = 0.782, η² = 0.004  EX \* HY: *p* = 0.514, η² = 0.023  <GNG - Accuracy>  Main effect EX: *p* = 0.001, η² = 0.467  Main effect HY: *p* = 0.972, η²` = 0.001  EX \* HY: *p* = 0.537, η² = 0.02 |

Note. N/A = Not Assessed, EX = Exercise, HY = Hypoxia, EX \* HY = Interaction effect between exercise and hypoxia, RCT = Randomized Controlled Trial, MTP = Multimodal Training Programs, IHHT = Interval Hypoxic – Hyperoxic Training, GNG = GO / NO-GO, ZVT = Zahlen Verbindungs Test, Spatial DR = Spatial Delayed Response, RMCPT = Running Memory Continuous Performance Task, CWST = Color-Word Stroop Task, DemTect = Dementia Detection Test, CDT = Clock-Drawing Test, MATH = Mathematical Performance, DET = Detection Task, IDN = Identification Task, OCL = One Card Learning Task

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| Table 2  Cognitive tasks and cognitive task categories. |
| **1. Information processing** |
| *a. Color-word Stroop task* |
| **2. Attention** |
| *a. d2 test (GZ, SKL)* |
| *b. Frankfurt Attention Inventory - 2* |
| **3. Executive function** |
| *a. GO/NO-GO task* |
| *b. Zahlen – Verbindungs – Test* |
| *c. Trail Making Test A and B* |
| *d. Flanker task* |
| *e. Mathematical performance* |
| *f. Interference control task* |
| **4. Memory** |
| *a. Spatial Delayed Response* |
| *b. Running Memory Continuous Performance Task* |
| *c. Memory recognition* |
| *d. N-back* |
| *e. One Card Learning Task* |
| *f. Dementia detection test* |
| *g. Clock-drawing test* |
| **5. Reaction time** |
| *a. Detection Task* |
| *b. Identification Task* |

Table 3

Exclusionary Criteria Table for Each of the Included Studies.

|  |  |
| --- | --- |
| **Study** | **Exclusionary Criteria** |
| [Ando, et al.3](#_ENREF_3) | · Participants who were currently engaged in regular training.  · Participants who had any history of cardiovascular, cerebrovascular, or respiratory disease. |
| [Schega, et al.32](#_ENREF_32) | · Subjects who were physically active and did not pass a medical examination by a medical doctor. |
| [Kim, et al.8](#_ENREF_8) | · Participants who had been exposed to normobaric hypoxia or altitudes over 2500m within previous 2 months.  · Participants who had any history of smoking or had signs of cardiovascular, metabolic, or respiratory disease.  · Participants who had experienced syncope, anemia, or fainting during exercise. |
| Komiyama, et al.16 | · Participants who had any history of cardiovascular, cerebrovascular, or respiratory diseases. |
| Seo, et al.45 | · Subjects who reported presence or history of pulmonary disease, cardiovascular disease, postural orthostatic  tachycardia syndrome, skeletal muscle injury in the lower limbs, and metabolic syndrome.  · Subjects who were exposed to normobaric hypoxia or an altitude above 2500m within 2 months before study. |
| Dobashi, et al.24 | · Participants who had any cardiovascular, cerebrovascular, or respiratory diseases.  · Participants who had smoked, taken mediation, or performed exercise training in the 6 months prior to study. |
| [Lefferts, et al.9](#_ENREF_9) | · Participants who had experienced smoking, hypertension, diabetes mellitus, hyperlipidemia, pulmonary disease,  renal disease, neurological disease, or peripheral artery disease. |
| [Schega, et al.33](#_ENREF_33) | · Participants who had stayed in an altitude above 1800m as well as blood donation in the last 2 months.  · Participants who had chronic or acute renal, cardiovascular, metabolic, neuronal or orthopaedic diseases. |
| Bayer, et al.58 | · Individuals who were inability to move unaided, uncontrolled hypertension (SBP > 180 mm Hg), chronic  bronchopulmonary diseases, decompensated heart failure (NYHA, Ⅲ-Ⅳ FC), previous intracerebral hemorrhages,  and marked cognitive disorders (MMSE < 12 points). |
| Bayer, et al.59 | · Subjects who were not able to walk without any staff assistance or suffered from severe dementia with a score of  Mini–Mental State Examination (MMSE) less than 12 points, uncontrolled hypertension (systolic blood  pressure[BP] > 180 mm Hg and/or diastolic BP > 100 mm Hg), COPD III–IV, decompensated heart failure  (NYHA III–IV), or previous intracerebral bleeding. |
| Komiyama, et al.23 | · Participants who had any history of cardiovascular, cerebrovascular, or respiratory disease. |
| [Seo, et al.10](#_ENREF_10) | · Subjects who not were physically active and had any history of pulmonary disease, cardiovascular disease, postural  orthostatic tachycardia syndrome, skeletal muscle injury in the lower limbs.  · Subjects who were exposed to hypoxia or an altitude above 2500m (8202 ft) within 2 months prior to study. |
| Stavres, et al.60 | · Subjects who were had any history of any cardiac, metabolic, or respiratory disease, any musculoskeletal issues  prohibiting exercise, or any previous adverse reaction to altitude exposure.  · Subjects had been to altitude (above 2500m) within 3 months prior to participating in study. |
| Limmer, et al.61 | · Subjects who had previous experience with the Frankfurt Attention InventoryÐ2 (FAIR-2) test, preceding altitude  sojourns above 2000m in the 4 weeks prior to the investigation, neurological disease, psychiatric illness, learning  disabilities, alcohol or drug use or any difficulty that could interfere with behavioral or cognitive testing. |
| Bayer, et al.62 | · Patients of the Geriatric Day Clinic who did not suffer from any diseases. |
| Lei, et al.17 | · Subjects who had not lived at altitude below 1300m.  · Subjects who had previous experience of hypoxic training or prior engagement in any regular exercise.  · Subjects who had experienced smoking and alcohol drinking habits.  · Subjects who had a self-reported regular menstrual cycle with 28-34 days of length.  · Subjects who were taking any form of the contraceptive pill or other drugs. |
| Morrison, et al.63 | · N /A |
| Sun, et al.18 | · Subjects who had not lived at altitude lower than 1000m.  · Subjects who had experience of hypoxic training and were currently engaged in any structured exercise.  · Subjects who were smokers and had taken oral contraceptives or any medication during the past 6 months.  · Subjects who had musculoskeletal problems. |

Note. N/A = Not Available

Table 4

Effect sizes by moderator variables in meta-ANOVA for Aim 1.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Category | *k* | SMD | 95% CI | Qь |
| **Sex** |  |  |  | 15.22\*\* |
| *Male* | 17 | -0.30\*\* | -0.48 to -0.11 |
| *Female* | 2 | 0.39\* | 0.09 to 0.69 |
| *Mixed* | 12 | 0.02 | -0.19 to 0.22 |
| **Age** |  |  |  | 2.01 |
| *Young Adults* | 21 | -0.20\* | -0.39 to 0.00 |
| *Older Adults* | 10 | 0.01 | -0.20 to 0.23 |
| **Cognitive task type** |  |  |  | 10.33\* |
| *Information processing* | 7 | 0.27 | 0.00 to 0.53 |
| *Attention* | 2 | -0.40 | -0.88 to 0.09 |
| *Executive function* | 12 | -0.18 | -0.39 to 0.02 |
| *Memory* | 10 | -0.26 | -0.55 to 0.04 |
| **Study design** |  |  |  | 2.38 |
| *RCT* | 12 | 0.02 | -0.19 to 0.22 |
| *NRS* | 19 | -0.21\* | -0.41 to -0.01 |

*Note. k* = Number of effect sizes; RCT = Randomized controlled trials; NRS = Non-randomized controlled studies;

CI = Confidence interval; Qь = Cochran’s Q statistics; \**p* < 0.05; \*\**p* < 0.01.

Table 5

Effect sizes by moderator variables in meta-ANOVA for Aim 2.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Category |  | *k* | SMD | 95%CI |  | Qь |
| **Sex** | |  |  |  | 2.96 | |
| *Male* | | 16 | 0.18 | -0.03 to 0.38 |
| *Female* | | 1 | 0.52 | -0.03 to 1.07 |
| *Mixed* | | 12 | 0.42\*\* | 0.19 to 0.65 |
| **Age** | |  |  |  | 6.30\* | |
| *Young Adults* | | 19 | 0.16 | -0.04 to 0.36 |
| *Older Adults* | | 10 | 0.51\*\* | 0.32 to 0.69 |
| **Cognitive task type** | |  |  |  | 9.34\* | |
| *Information processing* | | 7 | 0.26\* | 0.03 to 0.49 |
| *Attention* | | 2 | 0.78\*\* | 0.39 to 1.17 |
| *Executive function* | | 8 | 0.07 | -0.19 to 0.33 |
| *Memory* | | 12 | 0.38\*\* | 0.12 to 0.64 |
| **Study design** | |  |  |  | 1.98 | |
| *RCT* | | 12 | 0.42\*\* | 0.19 to 0.65 |
| *NRS* | | 17 | 0.20\* | 0.00 to 0.40 |
| **Exercise type** | |  |  |  | 17.12\*\* | |
| *Cycle ergometer* | | 21 | 0.23\*\* | 0.06 to 0.40 |
| *A full body strength-endurance program* | | 3 | 0.70\*\* | 0.39 to 1.01 |
| *Multimodal training program* | | 4 | 0.50\*\* | 0.14 to 0.85 |
| *Repeated sprint running* | | 1 | -0.71\* | -1.38 to -0.04 |
| **Exercise intensity** | |  |  |  | 3.98\* | |
| *Moderate* | | 26 | 0.36\*\* | 0.22 to 0.50 |
| *High* | | 3 | -0.41 | -1.16 to 0.34 |
| **Exercise temporality** | |  |  |  | 1.43 | |
| *During hypoxia* | | 8 | 0.45\*\* | 0.13 to 0.78 |
| *Both before and during hypoxia* | | 21 | 0.23\*\* | 0.06 to 0.40 |
| **Training type** | |  |  |  | 6.30\* | |
| *Acute exercise* | | 19 | 0.16 | -0.04 to 0.36 |
| *Chronic exercise* | | 10 | 0.51\*\* | 0.32 to 0.69 |

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| *Note. k* = Number of effect sizes; RCT = Randomized controlled trials; NRS = Non-randomized controlled studies;  CI = Confidence interval; Qь = Cochran’s Q statistics; \**p* < 0.05; \*\**p* < 0.01. |

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