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Original Paper

Research on the Impact of Altitude Hypoxia on Cognitive Function and the Enhancement of Hyperbaric Oxygen Intervention

Qing Xu

Tibet University, 850000, China

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Abstract

People's cognitive function is significantly influenced by the hypoxic environment at high altitudes. As elevation increases, reaching a certain threshold can exacerbate this effect. Hyperbaric oxygen therapy (HBOT) is a treatment for hypoxic conditions that involves breathing pure oxygen or high-concentration oxygen in an environment with pressure exceeding one atmosphere. Research has shown that HBOT can enhance cognitive function; however, there are limited studies focusing on individuals living in plateau regions. Compared to the low pressure and hypoxia experienced in lowland areas, HBOT offers greater therapeutic benefits in plateau regions. This paper summarizes the research on the impact of hypoxic environments on cognitive function at high altitudes and reviews the advancements in hyperbaric oxygen interventions. The aim is to explore the effectiveness of HBOT and to develop a research framework for optimizing oxygen dosage, which holds practical significance for promoting the health and well-being of people living in plateau areas.

Keywords

cognitive function, hypoxia environment, high altitude, hyperbaric oxygen intervention, oxygen dose

1. Introduction

Hypobaric hypoxia is a prominent characteristic of high-altitude environments. Generally, as altitude increases, air pressure decreases, resulting in thinner air. Additionally, temperatures in plateau regions can fluctuate significantly, leading to substantial temperature differences between day and night. Compared to lowland areas, plateaus experience longer periods of sunlight, drier climates, and increased radiation exposure. Consequently, many individuals from lower altitudes may experience altitude sickness upon their initial ascent to high altitudes, primarily due to hypoxia. Hypoxia is defined as a reduction in the partial pressure of oxygen in the alveoli. Although the brain constitutes only 2% of the human body weight, it requires approximately 25% glucose and about 20% oxygen to function normally (Hyder, Rothman, & Bennett, 2013). The human brain is particularly sensitive to hypoxia; under such conditions, cognitive functions, especially higher-order processes related to cognition, can be adversely affected (Li, Shi, Guo, Wang, & Wang, 2022). Hyperbaric oxygen therapy has been employed to treat various medical conditions, and numerous studies indicate that hyperbaric oxygen interventions can enhance cognitive function. Therefore, this paper reviews research on the impact of high-altitude hypoxic environments on cognitive function and the potential benefits of hyperbaric oxygen therapy in improving cognitive abilities. The aim is to explore the feasibility of hyperbaric oxygen interventions for enhancing cognitive function in hypoxic high-altitude regions and to identify directions for future optimization research.

2. The Effects of Altitude Hypoxia on Cognitive Function

Cognitive function refers to the performance of objective tasks that require conscious mental effort, including memory (encompassing language, spatial awareness, and working memory), attention, and executive function (Lamport, Saunders, Butler, & Spencer, 2014). Cognitive ability encompasses various skills such as spatial orientation, memory, reasoning, attention, language proficiency, and emotional processing (Beier & Oswald, 2012). Research has shown that hypoxia in high-altitude environments adversely affects cognitive function. As altitude increases, air pressure decreases, creating an anoxic environment that diminishes the accuracy of working memory and attention tasks. Changes in cognitive function may indicate subtle shifts in the neural and behavioral components of decision-making, aimed at reducing cognitive load and conserving brain resources in challenging environmental conditions (Lefferts, DeBlois, White et al., 2019).

2.1 Effect of Altitude Hypoxia on Attention

Attention refers to the direction and concentration of psychological activities or consciousness toward a specific object (Peng, 2019). Ma et al. (2017) discovered that long-term exposure to high altitudes negatively impacts the alertness and control levels of migrants' attention functions, while only affecting the orientation level of indigenous people living at elevations above 4,200 meter. An et al. (2017) found that the duration of residence at high altitudes influences executive control functions, suggesting a pattern of initial decline, followed by recovery, and then another decline over time. Wang et al. (2014) reported that prolonged exposure to high-altitude environments leads to hemispheric compensation during the early stages of identification, but reduces attention resources in later stages. Furthermore, the effects of altitude in the later stages are also influenced by perceived cognitive load.

2.2 Effect of Altitude Hypoxia on Working Memory

Working memory refers to a memory system with limited capacity that temporarily stores and processes information during cognitive tasks (Peng, 2019). A functional magnetic resonance imaging (fMRI) study indicated that, compared to residents at sea level, individuals at high altitudes exhibited longer reaction times and lower accuracy in behavioral performance. Additionally, activation in the inferior frontal gyrus, middle frontal gyrus, middle occipital gyrus, lingual gyrus, lumbar pyramid, and thalamus was reduced among high-altitude subjects. This suggests a decline in verbal working memory among residents at high altitudes (Yan, Zhang, Gong, & Weng, 2018). Similarly, other fMRI studies have shown a decrease in gray matter volume in the bilateral anterior insula, bilateral prefrontal cortex, left central frontal region, left cingulate gyrus, and right lingual cortex among high-altitude residents. Changes in anisotropy scores (FA) and regional homogeneity (ReHo) were also observed in correlation with these regions. High-altitude subjects performed poorly on a series of working memory tasks (Yan, Zhang, Shi, Gong, & Weng, 2010). Furthermore, other research has found that high-altitude residents exhibited strong activation in the left cone and left superior temporal gyrus, but weak activation in the left middle occipital gyrus. These brain regions are associated with working memory (Yan, Zhang, Gong, & Weng, 2011).

2.3 Effect of Altitude Hypoxia on Response Inhibition

Response inhibition refers to the ability to suppress irrelevant information that interferes with the current task, which is crucial for individuals to engage in goal-oriented behaviors in response to environmental changes (Logan & Cowan, 1984). Functional magnetic resonance imaging (fMRI) studies indicate that activation of the prefrontal cortex (PFC) and anterior cingulate cortex (ACC) is associated with response inhibition. Some studies have measured the N2 and P3 components of event-related potentials (ERP) in two groups of individuals: those who moved to high-altitude areas and those who lived in low-altitude areas, using a Go/No-Go task. The results revealed that the latency of NoGo-N2 was delayed in the high-altitude group compared to the low-altitude group. Additionally, under both Go and No-Go conditions, the N2 amplitude in the high-altitude group was larger, while the P3 amplitude was smaller compared to the low-altitude group. These findings suggest that exposure to high altitude affects response inhibition during the conflict monitoring stage, particularly in terms of processing speed (Ma, Wang, Wu, Luo, & Han, 2015). Long-term exposure to high-altitude environments may impair conflict control during the conflict resolution stage, leading to a reduction in the attentional resources available to high-altitude individuals for managing conflict.

3. Hyperbaric Oxygen Intervention

3.1 The Concept and Principles of Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) is a treatment method that involves exposure to pure oxygen under increased atmospheric pressure. Typically, a single treatment lasts between 1 to 1.5 hours, which includes approximately 15 minutes for pressurization and 15 minutes for decompression. Patients may undergo treatment once to three times a day, with a total of 20 to 60 therapeutic sessions depending on their condition. This method generally operates at pressures ranging from 2 to 3 atmospheres (Lee, Cha, & Lim, 2023). In contrast to standard oxygen supplementation, the physiological basis of HBOT in treating various diseases primarily lies in its ability to enhance blood oxygen tension and increase overall blood oxygen content (Wang, Cui, & Jin, 2009). By improving the diffusion rate of oxygen in the bloodstream and extending the effective diffusion distance of oxygen within tissues, HBOT can alleviate cognitive impairments associated with certain medical conditions by increasing tissue oxygenation. Under high pressure, the concentration of oxygen inhaled during HBOT can reach up to 99%, resulting in blood oxygen levels that are several times higher than those achieved with oxygen inhaled at normal pressure (Sun, Bao, An, et al., 2017). This treatment method incorporates a negative ion-generating device, which is non-invasive and non-toxic. By inhaling pure oxygen enriched with negative ions at high pressure, patients can stimulate the body's self-renewal processes and enhance cellular metabolism. Consequently, HBOT has evolved into an essential therapeutic approach for a variety of medical conditions and is widely recognized in the medical community both domestically and internationally (Sun, Bao, An, et al., 2017).

3.2 Study on the Influence of Hyperbaric Oxygen Therapy on Cognitive Function

In the earliest related research, 13 elderly male patients with cognitive impairment underwent 30 sessions of intermittent exposure to 100% oxygen at 2.5 absolute atmospheres. The study found that their cognitive function significantly improved following hyperbaric oxygen treatment (Jacobs, Winter, Alvis, & Small, 1969). Additional studies have examined the effects of hyperbaric oxygen (HBO) on the cognitive abilities of healthy adults using resting functional magnetic resonance imaging. These studies revealed that spatial working memory and memory quotient significantly increased after HBO exposure, suggesting that enhanced oxygen supply can improve memory capabilities to some extent (Yu, Wang, Li, Wang, Zhou, Chu, He, Wen, Ni, Liu, et al., 2015). A team of scientists from Israel conducted a series of hyperbaric oxygen experiments to investigate whether oxygen is a limiting factor in major cognitive domains among healthy young individuals. Fifty-six subjects were randomly assigned to either the HBO group or the normobaric oxygen group and underwent a series of tests to evaluate key cognitive areas, including information processing speed, situational memory, working memory, cognitive flexibility, and attention. The results indicated that, across all cognitive domains assessed, the scene memory of the HBO group showed statistically significant improvement, demonstrating a better learning curve and greater resistance to interference (Suzin, Frolinger, Yogev, Hadanny, Catalogna, Rassovsky, & Efrati, 2020). Furthermore, the researchers evaluated the impact of hyperbaric oxygen therapy (HBOT) on the cognitive function of healthy elderly individuals. In a randomized controlled clinical trial, 63 healthy adults were assigned to either the HBOT group or a control group for a three-month intervention. Cerebral blood flow (CBF) was assessed using magnetic resonance perfusion imaging. The findings confirmed that HBOT induces cognitive enhancement in healthy elderly individuals through mechanisms involving regional changes in CBF. The primary improvements observed included attention, information processing speed, and executive function, all of which typically decline with age (Hadanny, Malka, Gil, Rahav, Merav, Kobi, Yafit, Ramzia, Efrat, Gregory, et al., 2020).

At high altitudes, current research indicates that hyperbaric oxygen therapy (HBOT) can enhance cognitive function. Under conditions of high-altitude hypoxia, individuals experience a significant decrease in attention. However, with hyperbaric oxygen intervention, subjects demonstrate improved attention transfer ability and increased attention span (Bu, Yang, Zhang, & Ma, 2021). Additional studies have shown that the ability to adapt to hypoxia influences the working memory of plateau natives. A 30-minute hyperbaric oxygen intervention, administered ten times, has been found to enhance the working memory of these individuals (Wang, 2023). Based on the findings of this research, it is evident that a hyperbaric oxygen environment can improve cognitive abilities, making the application of HBOT highly valuable for those whose cognitive function is compromised.

3.3 Study on the Intervention Dose of Hyperbaric Oxygen

Although the current hyperbaric oxygen therapy typically involves breathing pure oxygen at pressures of 2 to 3 atmospheres, the duration of a single treatment can range from 1 to 1.5 hours. Depending on the patient's condition, 20 to 60 therapeutic sessions may be administered (Lee, Cha, & Lim, 2023). It is essential to discuss the optimal intervention plan tailored to various situations and environments, which includes considerations for dosage, frequency, and interval times, as well as strategies to minimize side effects to achieve maximum efficacy. Swiss toxicologist Paracelsus stated, "All substances in the world are toxic, and nothing is non-toxic. The difference between drugs and poisons lies in the appropriate dose." Therefore, it is crucial to investigate the relationship between oxygen dosage and human cellular response during hyperbaric oxygen therapy to enhance its effectiveness.

Leveque et al. (2023) investigated the metabolic reactions resulting from exposure to high pressure and elevated oxygen levels for one hour at 1.4 and 2.5 atmospheres. Blood samples were collected prior to exposure and at intervals of 30 minutes, 2 hours, 24 hours, and 48 hours post-exposure. The level of oxidation was assessed by measuring the rate of reactive oxygen species (ROS) production, nitric oxide metabolites (NOx), and the levels of isoprostane. Antioxidant responses were evaluated by quantifying superoxide dismutase (SOD), catalase (CAT), cysteine glycine, and glutathione (GSH). Interleukin-6, neopterin, and creatinine were utilized to assess the inflammatory response. Short-term (60 minutes) exposure to mild (1.4 ATA) and high (2.5 ATA) pressures resulted in a similar significant increase in reactive oxygen species and antioxidant responses. In contrast, Immunomodulation and the inflammatory response were found to be proportional to the dose of hyperbaric oxygen. Further research on dosage and recovery time between exposures is necessary to optimize the potential therapeutic benefits of this promising intervention.

4. Conclusion

Cognitive impairment caused by altitude hypoxia primarily affects working memory, attention, and reaction inhibition. Hyperbaric oxygen therapy, a method for treating hypoxic conditions, holds significant research potential in high-altitude regions. However, there are currently few studies focused on enhancing cognitive abilities in these areas through hyperbaric oxygen therapy. Future research could expand on this topic by optimizing the frequency and dosage of hyperbaric oxygen interventions to achieve maximum cognitive improvement while minimizing side effects. Additionally, more in-depth studies will contribute to addressing cognitive impairments resulting from hypoxic environments in high-altitude regions.

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