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The impact of hypoxia on psychological and cognitive functioning in high-altitude climbers

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Abstract

Introduction and purpose: This study aims to investigate the psychological and cognitive effects of hypoxia in high-altitude climbers, with a focus on specific psychological outcomes such as anxiety, hallucinations, and depression, and cognitive impairments, including memory deficits and impaired decision-making. The scope encompasses both acute and chronic exposure to high-altitude conditions, examining how hypoxia, in conjunction with environmental stressors such as cold, isolation, and physical exertion, impacts neurological function. The research seeks to elucidate the underlying mechanisms, including hypoxia-induced changes in cerebral oxygenation, neurotransmitter activity, and metabolic dysregulation, and their relationship to observed symptoms. By analyzing individual susceptibility, patterns of impairment, and potential mitigating factors, this study aims to contribute to a more comprehensive understanding of the impact of extreme environments on

psychological and cognitive health, with applications for improving climber safety and advancing neurophysiological research in hypoxic conditions.

Material and methods: An extensive examination of articles published in scientific journals was carried out using online research platforms databases, i.e. PubMed, Google Scholar, using key words contained in 'Medical Subject Headings' MeSH in appropriate configurations.

Description of the state of knowledge: Published data indicate that prolonged high-altitude exposure impairs cognitive performance, particularly in areas such as attention, memory, and inhibitory control. These deficits are linked to hypoxia-induced oxidative stress, mitochondrial dysfunction, and structural brain changes. However, certain cognitive domains, such as perceptual processes and problem-solving abilities, appear to remain relatively unaffected by high-altitude conditions.

Conclusions: Prolonged exposure to high altitudes detrimentally impacts cognitive performance. The most significant impairments are observed in psychomotor function and long-term memory. Perceptual processes, inhibitory control, and problem-solving skills are largely preserved. Further research is needed to explore individual variability and long-term adaptations to these environments.

Keywords: "hypoxia", "high-altitude climbers", "cognitive function"

Introduction

The effects of hypoxia on mental and cognitive health are of significant concern in high-altitude mountaineering, where extreme conditions exacerbate the physiological challenges posed by reduced oxygen availability. At elevations above 2,500 meters, hypoxia leads to impaired cerebral perfusion, altered neurotransmitter function, and disruptions in metabolic processes, all of which contribute to cognitive deficits. (1) Common manifestations of these impairments include decreased memory, slower reaction times, impaired attention, and compromised decision-making abilities. In more severe cases, high-altitude cerebral edema (HACE) can cause profound cognitive dysfunction, ataxia, and even loss of consciousness. These cognitive impairments not only threaten the safety of individuals in high-risk environments but also highlight the need for a deeper understanding of how hypoxia affects

brain function. Research into these effects is crucial for both improving mountaineering safety and advancing our understanding of brain health in hypoxic conditions. Insights gained from such studies can inform strategies to mitigate cognitive decline in extreme environments and have broader implications for medical and occupational settings where hypoxia is a concern.

Characteristics of High-Altitude Hypoxia

Physiological mechanisms

At high altitudes, oxygen transport is compromised due to the reduced partial pressure of oxygen in the environment. At sea level, oxygen binds to hemoglobin in red blood cells, forming oxyhemoglobin, which is then transported via the circulatory system to tissues. However, with decreasing atmospheric pressure at higher elevations, the oxygen content in the inspired air decreases, leading to lower oxygen saturation of hemoglobin. In response, the body initiates compensatory mechanisms, such as hyperventilation to increase the intake of oxygen and an increase in heart rate to enhance tissue perfusion. Over time, erythropoiesis is stimulated by elevated erythropoietin levels, which increases the number of red blood cells to improve oxygen-carrying capacity. (2)

Hemoglobin's affinity for oxygen (Hb-O_2 affinity) is a critical determinant of oxygen transport and delivery in the human body. This affinity is influenced by various factors, including pH levels, carbon dioxide concentration, temperature, and the presence of 2,3-bisphosphoglycerate (2,3-BPG). A rightward shift in the oxygen-hemoglobin dissociation curve indicates decreased affinity, facilitating oxygen release to tissues, while a leftward shift signifies increased affinity, enhancing oxygen uptake in the lungs. (3)

In high-altitude environments, where oxygen availability is reduced, the body adapts by modulating Hb-O_2 affinity to optimize oxygen delivery. Individuals with higher Hb-O_2 affinity exhibit attenuated increases in heart rate and erythropoietin production during hypoxic exposure, suggesting a more efficient physiological response to low oxygen conditions. (3)

When ascending to high altitudes, the oxygen dissociation curve shifts right at moderate altitudes due to increased levels of 2,3-DPG, which facilitates oxygen release. However, at extreme altitudes, the curve shifts left, driven by a reduction in CO2 levels in the blood. This

shift enhances oxygen binding, which is essential for oxygen uptake in the lungs when atmospheric oxygen is low. (4)

In cases of severe hypoxia, such as in high-altitude pulmonary edema (HAPE) or high-altitude cerebral edema (HACE), these adaptive responses become insufficient, leading to tissue hypoxia and organ dysfunction. These pathophysiological changes underscore the challenges of maintaining adequate oxygen transport and tissue oxygenation in hypoxic environments.

Stages of high-altitude illness

Altitude illness represents a continuum of pathophysiological responses to hypobaric hypoxia, primarily affecting individuals exposed to elevations above 2,500 meters. The initial and most prevalent manifestation is acute mountain sickness (AMS), characterized by nonspecific neurological symptoms such as cephalalgia, anorexia, dizziness, and general malaise, which are mediated by hypoxia-induced cerebral edema and increased intracranial pressure. (5) (6) Progression of AMS, if untreated, may result in more severe syndromes, including high-altitude pulmonary edema (HAPE) and high-altitude cerebral edema (HACE). HAPE is typified by noncardiogenic pulmonary edema caused by hypoxia-driven pulmonary vasoconstriction, presenting clinically with dyspnea, tachypnea, productive cough (often with frothy, blood-tinged sputum), and hypoxemia. HACE is a severe neurovascular condition characterized by cerebral edema, manifesting as progressive cognitive dysfunction, ataxia, and decreased levels of consciousness, which may culminate in coma or death. (7) Early recognition and immediate therapeutic interventions, such as descent to lower altitudes, supplemental oxygen, and pharmacological agents (e.g., dexamethasone, nifedipine), are imperative to mitigate morbidity and mortality. (8)

Table.1 Stages of high-altitude illness

Stage	Symptoms	Pathophysiology	Treatment
Acute Mountain Sickness (AMS)	Headache, nausea, dizziness, fatigue	Cerebral edema, hypoxia-induced effects on the brain	Rest, gradual descent, acetazolamide
High-Altitude Pulmonary Edema (HAPE)	Shortness of breath, cough (frothy sputum), cyanosis	Non-cardiogenic pulmonary edema due to hypoxic vasoconstriction	Descent, oxygen, nifedipine, diuretics

Stage	Symptoms	Pathophysiology	Treatment
High-Altitude Cerebral Edema (HACE)	Ataxia, confusion, loss of coordination, decreased consciousness	Severe cerebral edema leading to neurological deficits	Descent, dexamethasone, oxygen

High-altitude pulmonary edema (HAPE) typically develops before high-altitude cerebral edema (HACE) as a consequence of hypoxia-induced pulmonary vasoconstriction. However, both conditions may arise simultaneously in severe cases, as the systemic effects of hypoxia can lead to both pulmonary and cerebral complications. Timely diagnosis, rapid descent, and medical intervention, including oxygen therapy and pharmacological treatments (nifedipine for HAPE and dexamethasone for HACE), are essential for preventing progression to life-threatening stages. (9)

Drugs used for prevention and treatment of high-altitude illnesses

The most effective strategy for preventing acute mountain sickness (AMS), is a gradual and controlled ascent, which allows for physiological acclimatization to the reduced atmospheric oxygen levels. The Wilderness Medical Association recommends limiting the daily elevation gain to 500 meters when staying above 3,000 meters, emphasizing that the critical factor is the sleeping altitude, rather than the altitude reached during daytime activities. A rest day every 3–4 days at the same elevation further aids in acclimatization. (10)

In the majority of cases, AMS is self-limiting with sufficient rest, and pharmacological prophylaxis is typically not required for low-risk individuals. The main recommendation is to cease ascent until symptoms resolve. However, AMS can be partially mitigated through pharmacological intervention, with acetazolamide being the first-line treatment. Acetazolamide acts by inhibiting carbonic anhydrase in the kidneys, leading to enhanced bicarbonate excretion and inducing a mild metabolic acidosis**.** This counteracts the respiratory alkalosis caused by hyperventilation at high altitudes, thereby facilitating the acclimatization process. The recommended dosage is 250 mg/day**,** divided into two doses. (11)

In more severe cases of AMS, the addition of dexamethasone may be warranted due to its potent anti-inflammatory and cerebral edema-reducing effects. (10) Dexamethasone influences the expression of various genes involved in immune regulation, particularly those linked to inflammation. This includes genes responsible for the cytokine response, such as IL-1**,** IL-6**,** and TNF-α. By modifying these gene expressions, dexamethasone helps reduce cerebral edema and inflammation, key factors in treating HACE and other high-altitude complications. (12)

Table 2. Pharmacological treatment

Drug	Indication	Mechanism of Action	Dosage	Side Effects
Acetazolamide	Prevention and treatment of Acute Mountain Sickness (AMS)	Carbonic anhydrase inhibitor; induces metabolic acidosis to stimulate ventilation	125–250 mg twice daily	Tingling, frequent urination, nausea
Dexamethasone	Treatment of severe AMS and High-Altitude Cerebral Edema (HACE)	Corticosteroid; reduces inflammation and cerebral edema	4 mg every 6 hours	Insomnia, mood changes, hyperglycemia
Nifedipine	Prevention and treatment of High-Altitude Pulmonary Edema (HAPE)	Calcium channel blocker; reduces pulmonary artery pressure	30 mg extended-release every 12 hours	Dizziness, flushing, low blood pressure
Ibuprofen	Symptomatic relief of AMS-related headache	Nonsteroidal anti-inflammatory drug (NSAID); reduces inflammation and pain	400–600 mg every 6–8 hours	Gastrointestinal irritation, ulcers

(13) (8) (14)

Chronic hypoxia

Chronic hypoxia, as seen in populations residing at high altitudes, results in long-term physiological adaptations that differ significantly from the acute response to hypoxia. In acute hypoxia, the body's immediate compensatory mechanisms—such as hyperventilation, tachycardia, and the stimulation of erythropoiesis—serve to increase oxygen uptake and delivery. However, these responses are often insufficient to fully counteract the reduced oxygen availability, leading to a decrease in oxygen saturation of hemoglobin and potential progression to altitude-related illnesses like high-altitude pulmonary edema (HAPE) or high-altitude cerebral edema (HACE). In contrast, chronic hypoxia triggers a more profound and

sustained adaptation. Over time, there is a marked increase in red blood cell mass through persistent erythropoietin-mediated stimulation of erythropoiesis, which enhances the blood's oxygen-carrying capacity. Additionally, long-term exposure to low oxygen levels leads to structural changes, including increased capillary density, improved mitochondrial function, and enhanced tissue oxygen extraction, optimizing oxygen utilization. The hemoglobin-oxygen dissociation curve may also shift to facilitate better oxygen unloading at the tissue level. However, despite these adaptations, chronic hypoxia does not fully mitigate the impact of extreme hypoxic conditions, as the enhanced oxygen-carrying capacity remains limited by the intrinsic low oxygen availability, and individuals may still experience diminished exercise capacity, impaired cardiovascular function, and increased susceptibility to hypoxia-related disorders.

EEG biomarkers of cortical dysfunction in high-altitude hypoxia

Hypoxia-induced alterations in neural processing have been extensively studied using electroencephalography (EEG), revealing significant impacts on attention and working memory. Research indicates that hypoxia affects event-related potential (ERP) components differently depending on latency, suggesting a compensatory response. Prolonged exposure exacerbates these effects, resulting in compensatory delayed behavioral responses and alterations in behavioral monitoring and conflict inhibitory control, as reflected by reduced amplitudes in some attention-related ERP components, including N2, N2pc, and ERN. These findings highlight the critical role of hypoxia in cognitive function and integrity, with significant implications for psychopathological and neuropathological outcomes. (4) (15) (16)

Additionally, studies have shown that hypoxia can impair several cognitive domains such as attention, learning and memory, processing speed, and executive function, with the severity of cognitive deficits correlating with the duration and degree of hypoxia. (17) Recovery can be achieved after acute hypoxia, while sequelae or even dementia can be observed after chronic hypoxia, possibly due to different molecular mechanisms. (4)

Furthermore, EEG studies have identified specific neural alterations under hypoxic conditions. Research reports that hypoxia affects neural processing involved in orienting attention and analyzing target stimuli, altering ERP components such as ADAN, LDAP, P3a, MMN, and

P3b. (18) Inadequate oxygenation can lead to acute and chronic brain damage, with hypoxia affecting event-related potential components differently depending on latency. (4)

Electroencephalography (EEG) studies conducted on mountaineers ascending Mount Jade, Taiwan, reveal significant alterations in cortical activity associated with high-altitude exposure. The findings demonstrate an increase in theta wave power and a concurrent decrease in alpha wave power across multiple cortical regions, indicative of hypoxia-induced impairments in cortical function. (19) These changes reflect diminished attentional capacity and reduced cognitive efficiency, likely due to the brain's adaptive responses to low oxygen availability. Furthermore, the observed EEG patterns suggest slowed neural processing and heightened neural inefficiency, which may serve as early electrophysiological markers of neurological dysfunction under hypobaric hypoxic conditions. These results highlight the critical role of monitoring neurological function in high-altitude environments, particularly in populations at risk of hypoxia-related complications, and underscore the need for targeted preventive measures to mitigate cognitive and neural impairments. (20)

Psychological functioning in hypoxic conditions

Hallucinations

A field study conducted at Everest Base Camp (5,365 m) assessed psychotic symptoms among 99 climbers using the High Altitude Psychosis Questionnaire (HAPSY-Q) and the Prodromal Questionnaire, 16-items (PQ-16). The study revealed that while only one climber met the diagnostic criteria for psychosis according to the Mini International Neuropsychiatric Interview (M.I.N.I.), a significant number of participants reported subdiagnostic psychotic symptoms, with 10.3% endorsing items on the HAPSY-Q and 20.7% on the PQ-16. (21) This prevalence highlights the potential risks associated with psychotic symptoms in high-altitude environments, as even mild symptoms can increase the likelihood of accidents during climbs. (21) (22) In addition to hypoxia, several other factors can contribute to the occurrence of psychosis in high-altitude environments. These include sleep deprivation, physical exhaustion, dehydration, electrolyte imbalances, reduced visibility, feelings of isolation, and the perception of danger. Individuals engaging in extreme altitude activities may experience these

conditions as contributing stressors, even if they have no prior history of psychotic symptoms and do not experience them in subsequent exposures. (23) (24)

Depression

Animal studies have investigated the impact of high-altitude exposure on the occurrence of depressive disorders. There have been interesting findings reported on how exposure to moderate-high altitude (hypobaric hypoxia) affects depressive-like behaviors and inflammation in male and female rats. Findings showed increased inflammation markers, such as granulocyte:lymphocyte ratios and monocyte:lymphocyte ratios, and depressive behaviors, including anhedonia and immobility, particularly in female rats. It has been concluded that prolonged exposure to high altitude may contribute to depressive symptoms and inflammation, with implications for understanding the link between altitude, anxiety, depression, and suicidality. Further research is needed to explore causal mechanisms. (25)

Cognitive functioning in hypoxic conditions

Tab. 3 Mechanisms of cognitive decline

Mechanism	**Description**
Oxidative Stress	Chronic hypoxia leads to an imbalance between the production of reactive oxygen species and the body's antioxidant defences, resulting in oxidative stress that can damage brain cells and impair cognitive function.
Mitochondrial Dysfunction	High altitude exposure can cause mitochondrial dysfunction, which is linked to increased risks of mental health issues such as depression and anxiety, further contributing to cognitive decline.
Neuroinflammation	Prolonged hypoxia may trigger inflammatory responses in the brain, exacerbating cognitive impairments. (26)

Under hypoxic conditions, cognitive performance is significantly impacted, with the severity of impairment varying across different task types and levels of oxygen deprivation. Complex tasks, such as those involving memory, mathematical reasoning, and auditory monitoring,

show notable declines in performance, though they tend to recover relatively quickly, often within 20 minutes. (27) Attention and vigilance tasks, including reaction time assessments, experience slower normalization, with minor lapses in performance recovering within an hour, while more substantial impairments may persist for longer periods. Tasks requiring simple and choice reaction times typically recover within an hour, but tasks such as the PASAT[1], which involve mathematical reasoning, can show near-instantaneous recovery within 90 seconds. (28)

Simulated flight performance is particularly sensitive to hypoxia, with considerable disruptions in situational awareness and task execution observed for up to 10 minutes, even though these impairments are generally transient. Rapid sequential number reading shows near-immediate recovery within five minutes, whereas sustained attention and error monitoring tasks, such as the Conners' continuous performance test [2], exhibit recovery within 13–16 minutes. Importantly, the impact of hypoxia on cognitive function is not uniform—while some tasks recover more swiftly under moderate hypoxic conditions, more severe deprivation can prolong impairments, demonstrating the complexity of hypoxia's effects on cognitive functioning across various domains. (29)

[1] The PASAT (Paced Auditory Serial Addition Test) is a cognitive assessment measuring attention, concentration and information processing speed where participants listen to a series of numbers and must add each number to the one immediately preceding it, responding as quickly as possible without writing anything down, while the pace of the numbers gradually increases to test attention, concentration, and information processing speed. (30)

[2] The Conners' Continuous Performance Test (CPT) is a test used to measure attention and impulsivity. Participants are shown a series of stimuli (usually letters or numbers) on a screen and must respond to certain target stimuli (e.g., a specific letter or number) while ignoring others, assessing their ability to maintain focus and control impulsive responses over time. (31)

Decision-making challenges and risk judgement

Cognitive impairment resulting from hypoxia at high altitudes poses a significant risk to mountaineers, often leading to poor judgment and increased risk-taking behavior. A case study published in *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery* described a climber who, following a high-altitude ascent without adequate preparation against acute hypoxia, exhibited persistent neuropsychiatric symptoms consistent with frontotemporal dementia, likely contributing to impaired decision-making during the climb. (4) Similarly, a meta-analysis in the *International Journal of Environmental Research and Public Health* highlighted that high-altitude mountaineering negatively impacts cognitive functions such as short-term memory, attention, and judgment. These deficits substantially elevate the risk of accidents, including falls, frostbite, and fatigue-related incidents, potentially leading to fatal outcomes. These findings emphasize the critical need for proper acclimatization and cognitive monitoring during high-altitude expeditions to reduce risks associated with impaired judgment and decision-making. (32)

Climbers' persistence in continuing their ascent despite the inherent risks and the availability of safer alternatives, such as descending, can be understood through several psychological mechanisms that influence decision-making and risk assessment. One key factor is overconfidence bias**,** which leads climbers to overestimate their abilities and underestimate the risks involved, resulting in an inflated sense of control over potentially dangerous situations. This bias, coupled with optimism bias**,** contributes to the belief that negative outcomes, such as accidents or failure, are less likely to occur to them compared to others, thus encouraging further progression despite worsening conditions. Another significant influence is escalation of commitment, often referred to as the sunk cost fallacy. In high-risk situations, climbers may feel psychologically compelled to continue their climb after already investing significant time, energy, and resources, leading to a reluctance to abandon the goal. Hypoxia**,** or reduced oxygen levels at high altitudes, exacerbates these biases, as climbers may experience cognitive impairments such as reduced attention, judgment, and decision-making abilities, further skewing their risk perception. (33) Hypoxia can induce a sense of euphoria or a false sense of invulnerability, diminishing the perceived threat of continuing the ascent. Additionally, climbers often experience a flow state**,** a condition characterized by deep concentration and engagement, where they become absorbed in the task at hand to the exclusion of external risks. This cognitive narrowing, compounded by hypoxia, can impair their ability to assess and respond to potential hazards in the environment. Furthermore, social

dynamics, including groupthink**,** may exacerbate this persistence. Climbers may suppress safety concerns and adopt a more risk-tolerant mindset to maintain group cohesion and avoid appearing weak, which can contribute to dangerous decision-making. These psychological mechanisms, interacting with the cognitive and physiological impairments caused by hypoxia, work together to influence climbers' behavior and decision-making processes in ways that may lead to continued risk-taking, even when descending would be the safer choice. (34)

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