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*Narrative Review*

# High Altitude Neurology

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## 1. Introduction

High Altitude (HA) attracts a large number of people, including travelers, athletes, and military personnel. However, the HA environment is a serious challenge for these people living at lower altitudes. Especially, neurological dysfunction, including cognitive function decline, equilibrium, and sleep disorders are common symptoms for people entering HA. While it is generally possible for individuals with neurological disturbances to go trekking, it is important to consider several factors before embarking on trekking that involve physical exertion, exposure to various environmental conditions, and potential challenges along the trail. Therefore, it is crucial to assess the specific condition and consult with a healthcare professional who can provide personalized advice based on individual circumstances.

Factors to consider include in consultation before planning any trekking trip, it is essential to review with a healthcare professional familiar with the neurological condition being managed. Understanding the neuropsychiatric status for such conditions and limitations: it is crucial to have a clear understanding of the specific neurological condition and its impact on physical capabilities. Some neurological conditions are contraindicated in HA and trekking should be banned. At HA, the reduced oxygen availability can have various effects on the central nervous system (CNS) and its interactions with mitochondria. There are some potential aspects of CNS dysfunction related to mitochondria at HA:

## 2. Oxidative Stress

Reduced oxygen levels at high altitudes can lead to an imbalance between the production and clearance of reactive oxygen species (ROS) in mitochondria. Excessive ROS can cause oxidative stress, damaging cellular components, including those in the CNS. This oxidative stress may contribute to CNS dysfunction.

## 3. Mitochondrial Dysfunction

Hypoxia can directly affect mitochondrial function in neurons, muscle, and other cells. Mitochondrial oxidative phosphorylation may be compromised, leading to reduced ATP production and impaired energy metabolism. Mitochondrial dysfunction may disrupt neuronal signaling, synaptic transmission, and overall CNS function.

## 4. Blood-Brain Barrier (BBB) Disruption

The BBB protects the brain from harmful substances circulating in the bloodstream. Hypoxia-induced oxidative stress can impair BBB integrity and function, allowing the entry of toxins and inflammatory molecules into the CNS. These harmful substances can exacerbate mitochondrial dysfunction and CNS dysfunction.

## 5. Neurodegenerative Diseases

Prolonged exposure to high altitudes has been associated with an increased risk of neurodegenerative diseases such as Alzheimer's and Parkinson's disease. It is important to note that the precise mechanisms and extent of CNS dysfunction related to mitochondria at high altitudes are still being investigated. Various factors, including individual susceptibility, duration of exposure, and acclimatization, can influence the impact of high-altitude hypoxia.

Metabolic studies suggest that with high altitude hypoxia, there is impairment in neurotransmitters and the blood-brain barrier in hypoxia does not function well. Transcranial ultrasound

and MRI studies demonstrated an increase in the MCA diameter on acute exposure to both normobaric and hypobaric hypoxia[1,2]. In acclimatized people no evidence of cerebral artery vasodilation was shown up to 6400m above this altitude vasodilation occurs and it is reversed rapidly with supplementary oxygen[3,4].

Another contributing factor is nocturnal hypoxemia: on the first night of arrival at altitude there is extreme hypoxemia during sleep, this might emphasize the possible danger for many patients if they have pre-existing hypercapnia or a low ventilatory drive.

## 5.1. Migraine

There is an observed higher incidence of migraine attacks at altitude. Every mountaineer with migraine knows that at altitude his headache can increase in frequency and intensity[5]. It is clear why high altitude is a migraine trigger since it seems to activate the trigeminovascular system, and beyond this, there is an increased cerebral blood flow at altitude[6]. Both migraine and AMS could be possibly attributed to an activation of the trigeminovascular system which is a very important sensory input[7]. Signals generated at high altitudes which may activate the trigemino-vascular system include proteins and neurotransmitters. Headache can be attributed to the activation of a common pathway in the trigemino-vascular system by both biochemical and mechanical stimulation.

The effects of triptans act both on vasoconstriction and since they have an action on brainstem serotoninergic nuclei. The use of triptans seems to be safe and recent studies also suggest some usefulness in AMS prevention[8]. In a recent Cochrane review, the quality of evidence for the latter study has been degraded to a low quality due to imprecision[8,9]. Migraine Recommendations In case of migraine with atypical or prolonged aura, we recommend before travel:

Brain MRI with diffusion-weighted study to disclose recent embolic subclinical strokes Blood analysis to study thrombophilic states such as protein C or S. Any patient who suffers from migraines must be informed that their headaches can worsen at altitude, both in frequency and/or intensity. Migraine patients should have in their backpack a proven effective drug (aspirin, FANS, or triptans) and a second drug for potential prevention treatment (e.g. flunarizine or amitriptyline) Cerebrovascular disease.

Stroke is the third cause of death and the first disability in developed countries. In Italy, a recent study showed a slight reduction in stroke incidence[11]. About one-third of stroke patients manage to maintain their independence without disability or with slight disability and resume normal activities, including traveling or recreational activities at altitude.

Like skiing or trekking Scientific literature has reported case studies of possible severe strokes at altitude[11,12] in healthy people. There is some research on the incidence of experiencing a first-ever stroke at altitude, but studies evaluating the incidence of recurrent stroke are lacking. One study on Indian soldiers showed that hospitalization at high altitudes for first-ever stroke was more frequent (13.7/1000 versus 1.05/1000) and that stroke incidence might be higher above 3500m[13]. According to Kumar[14,15], a long-term stay at a high altitude is associated with a higher risk of stroke. Although all types of stroke were seen, ischemic stroke was the commonest. Massive infarcts were common. Polycythemia might represent an important risk factor. However, in a letter in response to a similar observation by Saed, Falla, et al.[15] reached different conclusions, and the risk of stroke in high-altitude populations needs further assessment. Several factors that occur at high altitudes can explain the possible risk increase, especially dehydration and polycythemia with consequent "inspissatio sanguinis"[16]. Hypoxia can trigger endothelial dysfunction coagulation abnormalities and platelet aggregation[17]. The use of a recent oral anticoagulant is a valuable addition.

Long-term stays at high altitudes in association with a hypercoagulable state - in particular, congenital or acquired thrombophilia - appear to predispose to cerebral venous thrombosis (CVT). The association of CVT with a single exposure to high altitude seems low, but the risk cannot as yet be specifically estimated [18]. Altitude may induce larger infarcts for the concomitant hypoxia and therefore expose people to a higher risk of death [11]. Moreover, some research suggests the effects of hypoxia on cerebral circulation with altered cerebrovascular reactivity on the field[19] or in the hypobaric chamber couch[20].

It is not clear what the embolic risk at altitude is. In one experimental study, hypobaric hypoxia caused aseptic vegetation on heart valves in rats after 36 hours of exposure[20]. Patent foramen ovale (PFO) or another right to left shunts are possible risk factors for embolic stroke at altitude[21]. On the other hand, recent data[22] suggest that in climbers that developed AMS, there is a higher prevalence of PFO carriers (63%) while in non-AMS climbers only 39% had PFO. Clinicians should consider PFO as a risk factor for AMS during climbing. These worsened during exercise[2] and were diagnosed in a hypobaric chamber when 3 patients suffered TIAs at extreme altitudes[20]. Hypoxia can finally induce cardiac arrhythmias[23]. It is well known that altered cerebrovascular reactivity might confer an increased risk of stroke[24] in almost any patient with pre-existing vascular risk factors such as arterial hypertension[25], diabetes mellitus[26], carotid stenosis[27], in people with white matter leukoencephalopathy[28] and in a patient with previous recent stroke.

From the epidemiological and clinical point of view, the risk of a second stroke after the first ever stroke is high for at least one year[29]; after a TIA the risk of stroke and other vascular problems including vascular death is 8% at 30 days and 9.2% at 90 days[29-31].

We know that such patients are at a higher risk of developing CVA in the 3 months after the one they suffered a TIA[30]. All treatable risk factors should be first treated (such as severe carotid stenosis, blood pressure, other cardiac sources of emboli, etc.). Moreover, we also recommend checking cholesterol HDL/LDL, C-reactive protein, and homocysteine levels, all markers of endothelial damage. The patient should continue treatment with antiplatelet drugs and should be advised to not exceed altitudes over 3000 m[31].

Transient Ischemic Attacks (TIA) this is defined as a focal neurological deficit lasting less than 24 hours[30]. The diagnosis has to be done by a neurologist (isolated vertigo or syncope are not TIAs). It is therefore advisable that a mountaineer with a possible TIA needs first a cerebrovascular workup. In the mountains, a pragmatic alternative is to start treatment with aspirin.

Tumors and other lesions Patients with intracranial lesions are neurologically unstable and should not travel to altitude[32].

Several explanations and case reports support this advice. According to the Monroe-Kellie doctrine, any increase in any one of the volumes of the brain, blood, or cerebrospinal fluid volume (CSF) is compensated with the reduction of the other two; however, once these compensative measures are exhausted, an elevation of intracranial pressure (ICP) occurs. Indeed, cerebral edema that occurs at high altitudes is reflected by an increased tissue water content and swelling of perivascular glial end feet. There are reports of brain tumors both malignant and benign which suddenly become symptomatic when people are exposed to high altitude[33,34] or during long commercial flights[36-38]. This might be due to edema, an increase in cerebral blood flow, or increased cerebrospinal fluid pressure. A similar problem is presented by arachnoidal cysts[39].

Brain trauma, head concussion, and metabolic dysfunction The time required for the brain repair itself following a common brain trauma is not well understood, especially at HA where the brain repair resulting from a concussion is likely to be slow. Indirect evidence suggests that an increased blood-brain permeability enhancing the action of free radicals is possible.

It is also known that hypoxia is one of the possible secondary insults that affect short and long-term outcomes and is associated with poorer neurological outcomes in traumatic brain injury (TBI) patients[40]. In addition, elevated hemoglobin concentration due to chronic hypoxic exposure, commonly present in long-lived inhabitants of the Tibetan plateau region, has been shown to have a deleterious effect on recovery and mortality of patients with acute severe head trauma after decompressive craniectomy[41]. In conclusion, for a patient with a traumatic or metabolic brain injury (such as CO poisoning) previous brain hypoxia, or metabolic dysfunction after a cardiovascular operation, it does not seem advisable to go at high altitude.

### 5.2. Multiple sclerosis (MS)

Patients with MS might be considered safe up to 2500 meters. MS patients may develop new neurological signs and symptoms if they present an infection or if exposed to a cold; moreover, an exacerbation of a relapsing-remitting MS was recently reported with exposure to high altitude (Mt. Fuji at 3.776 meters)[42].

MS is an autoimmune disease and repetitive proinflammatory cascades could also act at the endothelial level causing decreased vasodilatory capacity, which limits blood supply for neurons performing demanding tasks and therefore leads to the overproduction of nitric oxide, which, in turn, contributes to the secondary neurons degenerative damage[43].

Dicianno, et al. found, at the National Veterans Winter Sports Clinic in Colorado (elevation between 2470 and 3813 meters), that athletes with several neurological disabilities (spinal cord injury, traumatic brain injury, multiple sclerosis, stroke, and other neurological impairments)[44], an overall higher occurrence of AMS and particularly in 3 of the 5 athletes with multiple sclerosis (60%)[45]. Subsequently, they reported in 2013 data collected over three years (2007, 2008, and 2009) with a higher number of participants and they found that athletes with neurological impairment showed a higher mean Lake Louise Score (LLS) compared to healthy controls and that the presence of neurological impairment, prior history of AMS and prior history of headache at HA were correlated with higher LLS[46].

Mitochondria exercise at high altitude Mitochondria produce energy in the form of ATP through oxidative phosphorylation. High-altitude environments have lower oxygen levels compared to sea level. During exposure to HA, oxygen availability decreases, leading to a reduced oxygen supply to the body's tissues.

Reduced oxygen levels can impair mitochondrial function and lead to a shift in cellular metabolism. In response to hypoxia, the mitochondria undergo several adaptations to optimize energy production and maintain cellular homeostasis. One key adaptation is thought to be an increase in the number and size of mitochondria. This increase, known as mitochondrial biogenesis, is regulated by various signaling pathways, such as the hypoxia-inducible factor (HIF) pathway.

Additionally, in hypoxic conditions, the mitochondria may switch to alternative metabolic pathways to generate ATP. For example, anaerobic glycolysis becomes more prominent, producing ATP but with a lower efficiency compared to oxidative phosphorylation. Mitochondrial damage is often present and leads to the "lactate paradox".

Moreover, mitochondria play a crucial role in the production of reactive oxygen species (ROS), which are byproducts of oxygen metabolism. In hypoxic conditions, the imbalance between ROS production and clearance can occur, resulting in oxidative stress. This oxidative stress can damage the mitochondria and other cellular components, leading to various physiological consequences. The mitochondrial adaptations aim to maintain cellular energy production and homeostasis under low oxygen conditions.

Aerobic activities, such as running, biking, and swimming will improve your VO2 max: the maximum volume of oxygen that your body can use. This is important for a high-altitude trek as there will be less oxygen in the air for you to consume and each breath has to count. This has been exploited in several conditions (**Figure 1**), basically there are four different conditions for exercise training. HA training can potentially improve your endurance during intense exercise. It may increase your aerobic capacity, lactic acid tolerance, and oxygen flow to your muscles. To prevent altitude sickness, climb slowly and reduce your intensity at high altitudes.

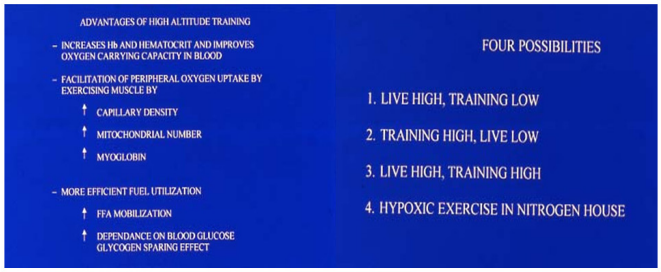


**Figure 1:** Hypoxia use for high altitude training.

Peripheral nerve disorders and neuromuscular diseases: Sarcopenia in HA Sarcopenia is a condition characterized by the loss of muscle mass, strength, and function that occurs with aging, however, sarcopenia occurs at HA. While sarcopenia is primarily associated with age-related factors such as reduced physical activity and hormonal changes, there may be additional considerations in individuals living at high altitudes.

HA environments present unique challenges to the human body, including decreased oxygen availability, changes in atmospheric pressure, and increased energy demands. These factors can have various effects on muscle physiology, potentially exacerbating the development or progression of

sarcopenia. Factors to be considered are: Hypoxia can contribute to muscle wasting and loss of muscle strength. Reduced oxygen availability impairs muscle protein synthesis and increases protein breakdown, potentially accelerating muscle wasting.

Living at high altitudes often requires individuals to adapt to physical and physiological changes. Adjusting to a HA environment can lead to a decrease in physical activity levels, resulting in muscle disuse and atrophy. Adequate nutrition is essential for maintaining muscle mass and function. Changes in appetite, increased metabolic demands, and altered nutrient availability at high altitudes can impact dietary intake. If individuals do not consume adequate protein and energy, it may contribute to muscle loss and sarcopenia. To mitigate the potential effects of HA environments on sarcopenia, it is essential to focus on key strategies: engaging in appropriate resistance training exercises can help preserve muscle mass and strength. Exercises that target major muscle groups can be effective in combating muscle loss.

### 5.3. Balanced nutrition

Consuming a well-balanced diet rich in high-quality protein, essential nutrients, and adequate calories is crucial. Adequate protein intake, particularly from sources like lean meats, fish, dairy, and plant-based proteins, can support muscle maintenance and repair.

### 5.4. Oxygen supplementation

In extreme cases, supplemental oxygen might be necessary to alleviate symptoms of hypoxia and improve exercise tolerance. Working with healthcare professionals, such as physicians, nutritionists, and exercise specialists, can help develop personalized interventions and strategies for managing sarcopenia at HA. It's important to note that while these recommendations may be beneficial, studies specifically assessing the impact of HA on sarcopenia are limited.

In sensory-motor peripheral neuropathies, both inherited or acquired there is risk related to the relative insensitivity of the foot during walking or climbing. In diabetic neuropathy, there is in addition a microvascular abnormality[47]. Such patients must wear comfortable shoes that are not tight to help promote a continuous blood flow to peripheral extremities since the activity of skeletal muscles and their body temperature is critical. When purchasing climbing shoes find a climbing shoe that fits the shape of your feet, including existing deformities. Foot size may also be slightly larger in hot weather, after standing for some hours, during the menstrual cycle, or at altitude where there is slight edema in the feet of women.

People should stay hydrated, avoid immobility to prevent deep venous thrombosis, and walk with warm comfortable stockings for mountaineering, and flight socks when flying. There is no evidence that previous peripheral damage can progress at altitude. Paulson et al. found that Charcot Marie Tooth patients were at risk of developing dysarthria, incoordination, and difficulty walking after returning from skiing at 8000 ft in the Colorado mountains[48].

Many patients with muscular dystrophies, such as Becker's, limb-girdle muscular dystrophy or myotonic dystrophy, and amyotrophic lateral sclerosis, can have alveolar hypoventilation with hypoxemia and sleep disturbances, including sleep apnoea, with consequent nocturnal hypoxemia that arrives at oxygen saturations as low as 75% at sea level. It is easy to imagine that these patients can have more desaturations at altitude. Therefore, patients with neuromuscular disorders should be screened for the presence of sleep apnoea before traveling at high altitudes and, if sleep disturbance is detected, they should travel with non-invasive ventilatory support[49].

## 6. Seizures at Altitude

There are case reports of new onsets of seizures at high altitudes outside the usual setting of AMS or HACE[50], as well as the occurrence of seizures in persons with a remote history of fits without therapy[51] or in treatment with antiepileptic drugs[52]. Two male trekkers in Nepal presented a single generalized grand mal seizure with tonic-clonic jerks, tongue bites, and post-ictal confusion[53]. Extensive medical investigations in Kathmandu including CT and EEG did not reveal any abnormality and both were seizure-free in the following years. The pathophysiology of these single seizures was unlikely related to AMS or HACE since both mountaineers had adequate acclimatization. Seizures may result from any physiological event determining an increase in neuronal excitability including shortage of sleep, exhaustion, dehydration, and electrolyte disturbances such as hypocalcemia or hyponatremia[53]. Acute severe hypoxia may cause epileptic seizures (see case report for DD). De novo seizures in people at altitude are anecdotal but may be fatal[51].

Observations on seizures at altitude are: in hypoxia, some GM crises have been reported they tend to be first-time fits, they occur in the first 2-3 days after arrival, and there is an underrepresentation of alcohol abuse. For known epileptics it is advisable to stay on previous antiepileptic medicine at altitude[52], avoid lack of sleep and alcohol use, and avoid also epileptogenic drugs; if they discarded therapy one should consider resuming medicines. In persons with seizure disorders exacerbations possibly due to altitude or lack of sleep have been observed, at least in those not on medication.

## 7. Dementia and MCI

Higher cortical function which includes cognitive and psychiatric aspects has been reported to be affected by acute or chronic altitude exposure in normal subjects[54]. It is also known that hypoxemia is a crucial factor for cognitive impairment in patients with pulmonary[55,56] and cardiopulmonary disorders[57,58] and that the degree of cognitive impairments is closely related to the degree of hypoxia. Available recommendations have been given for HA travelers[59].

Andean HA dwellers compared to lowlanders showed a slightly impaired cognitive function[60-62]. However, in a study performed in less developed areas of sub-Saharan Africa and South Asia on 481 residents at altitude (between 2100 m and 4000 m asl) aged > 60-years who underwent a cognitive screen, 1.37% were classified as cases of Mild Cognitive Impairment (MCI) whereas the 98.8% of people scored within normal range. The contradictory results may depend in the latter case on specific population characteristics (e.g. illiterate) but also could be related to the reduced environmental and cardiovascular risk factors in such populations[63]. Due to the potential deleterious effect exerted by hypoxia on cognitive functions, it is not advised HA, this applies also to MCI patients. MCI is a condition in which individuals demonstrate cognitive impairment with minimal impairment of instrumental activities of daily living and is considered to be an intermediate state between normal cognitive aging and early dementia[64]. However, many individuals are found to be cognitively normal in follow-up assessments and a meta-analy-

sis that assessed reversion rates in 25 studies indicated an overall reversion rate of approximately 24%[65]. Several factors (e.g., lifestyle) have been implicated in MCI reversion. However, it is not yet established whether hypoxia exposure may contribute to the progression of MCI into dementia. Experimental intermittent hypoxia (IH)-hyperoxia training has demonstrated improvement in cognitive functions and decreased Alzheimer's disease (AD) biomarkers in MCI patients[66].

## 8. Parkinson's Disease (PD)

PD is related to the neurodegeneration of the nigrostriatal dopamine system which leads to a decreased dopaminergic transmission in the basal ganglia. Basal ganglia are particularly susceptible to hypoxia-ischemia due to their high metabolic activity[67]. HIF is known to play an important role in the pathogenesis of neurodegenerative disorders and has been suggested to contribute to PD pathogenesis[68]. Impaired chemo sensitivity to hypoxia and perception of dyspnoea was also reported in PD patients[69]. Recently has also been reported that chronic intermittent hypoxia due to obstructive sleep apnea syndrome (OSAS) contributes to the pathogenesis of PD increasing the a-synuclein levels[70]. Moreover, the possible involvement of the autonomic nervous system in patients with PD may lead to the lack of compensatory mechanisms with exposure to altitude.

One case of Parkinsonism after acute hypobaric hypoxia exposure (up to 16,000 ft - 4,877 m) resulting in damage to the basal ganglia has been reported[71]. However, there are no published data in the literature regarding patients with idiopathic PD traveling to altitude. Few studies were performed to evaluate the effects of a mountain exercise in PD patients and demonstrate improvement in motor performance and social cognition, however, it is not specified at which altitude they stayed[72,73].

With the abovementioned premises, screening for the presence of sleep apnoea is advisable before traveling at high altitudes and, if sleep disturbance is detected, they should travel with non-invasive ventilatory support[48]. Risk factors known to be related to altitude exposure should be assessed in PD patients (e.g., prior history of AMS, prior history of headache at HA, etc.) and specific recommendations are that every Parkinsonian patient needs always to visit the mountain accompanied, needs to maintain adequate hydration and to have their specific oral antiparkinsonian drugs promptly available. For cases of neurological conditions like Parkinson's disease and Multiple sclerosis, poles without the traditional Nordic walking strap may be preferable. Fitness walking poles that are specially designed to provide an upright posture and additional support can be ideal and as the walker is not strapped in safer too. In some cases, it is not advised that the user is strapped to the pole at all as it can increase the possibility of trips and falls and in some instances, they might cause additional injury should they ever actually fall COVID-19 (or SARS-CoV-2) infection and neurological complications Recent evidence has shown that COVID-19 can determine several neurological dysfunctions such as hyposmia[74], Guillain-Barré syndrome[75], CNS lesions, impaired consciousness, and thrombosis[76,77]. Therefore, people who have had COVID-19 infection should be examined by a neurologist. On the other hand, it has been reported a possible lower incidence of COVID-19 at high altitudes according to epidemiological data[78,79]. However, these data should be considered preliminary and speculative as it has been discussed in a recent paper by Pun, et al.[80].

Pulmonary infection in COVID-19 although similar has different pathogenic mechanisms from HAPE[81]. It is unknown if previous COVID-19 infection predisposes to AMS, HACE, or HAPE.

## 9. Mood and Psychiatric Disorders

People with mood disorders (depression, bipolar disorders, etc.) are sometimes unaware of such complications. Medical professionals and mountaineers should be aware of somatic complications of HA exposure, but research, clinical guidelines, and knowledge among mountaineers concerning mental symptoms of HA are limited. Psychopathological changes, such as altered consciousness or attention, hallucinations, and delusions can occur at HA during trekking[82] and are known as the phenomenon of hallucinations after Everest climbing. These changes have most commonly been linked not only to underlying organic processes triggered by hypoxia but also to infections, environmental conditions, or drugs[83]. Psychogenic factors such as social isolation or mental stress may also play a role.

People with several psychiatric conditions go trekking and even will benefit from it. Trekking can be an enjoyable and rewarding experience for individuals with psychiatric conditions. However, it is important to approach trekking with careful consideration and preparation, taking into account the specific challenges that may arise. Here are some factors to consider: before planning a trekking trip, it is advisable to consult with a mental health professional who is familiar with the individual's condition. They can provide guidance and assess the suitability of trekking based on the individual's mental health status, coping mechanisms, and any potential risks. Understanding personal limitations: It is crucial to have a realistic understanding of one's mental health condition and limitations. Consider how symptoms such as anxiety, depression, or mood fluctuations may be triggered or influenced by the physical exertion or environmental conditions encountered during trekking. Trekking should be enjoyable and well-planned, psychotic episodes or conflicts can happen.

In aviation medicine is difficult to diagnose, as early as possible, pilots with psychiatric disorders that may impair pilot performance and increase the risk of incidents and accidents[84]. This diagnosis applies particularly to bipolar disorder (BD), where return to flying duty is not an option in the majority of cases. BD is a long-term mental disorder presenting remittent depressive, hypomanic, manic, or mixed episodes between low symptomatic or asymptomatic intermediate periods. Onset in most cases is in the late teen or early adult years. Suicidal intentions and suicide risk are significantly elevated in individuals with BD compared to the general population.

## 10. Sleep Disturbances

During a Nepal trek, sleep disorders occurred in over 50% of participants, with nightmare episodes. Sleep is a cornerstone for maintaining physiological homeostasis. Modifications of sleep due to changes in schedule, duration, dark-light cycle, and oxygen availability may result in decreased physical and cognitive performance. Among these factors, oxygen availability, particularly in the form of hypobaric hypoxia, calls for more attention given the increasing exposure of humans to HA environments.

Sleep can be challenging at HA due to decreased oxygen levels lower air pressure, and other factors specific to the high-al-

titude environment. Here are some tips to improve your sleep quality at high altitudes. Gradual acclimatization: Give the body adequate time to adjust to HA. It is generally recommended to ascend slowly, allowing for proper acclimatization at intermediate altitudes before going higher. Hydration: stay hydrated by drinking plenty of water. Dehydration can worsen the symptoms of altitude sickness, which may negatively affect your sleep. Avoid excessive alcohol and caffeine consumption as they can contribute to dehydration.

Maintain a balanced diet with sufficient calories and nutrients. Adequate nutrition can help support your body's adaptation to the altitude and promote better sleep. Engage in light physical activity and avoid strenuous exercise, especially during the first couple of days, avoid alcohol intake and benzodiazepine use. Periodic breathing due to altitudinal hypoxia is a respiratory event that has been previously described both under field and laboratory conditions during nighttime sleep. During its nocturnal presentation, periodic breathing has an accentuated sex-dependent incidence, being predominantly a male phenomenon. This could be explained either by an inhibitory effect of female hormones or a trigger effect of testosterone according to Rivera-Riveros[85].

## 11. Conclusion

"The mountains are calling, and I must go" was the reason given by the famous mountaineer John Muir encapsulating how individuals are attracted to outdoor sports. He has described wonderful paths in the Sierra in California. Several studies have shown that physical activity, especially in outdoor environments, might exert a positive effect on physical and mental health. Regular exercise enhances general physical well-being, and mood, and reduces anxiety, whereas reduced physical activity is affiliated with chronic disease, according to a study[86] regular and extreme mountaineering can show characteristic properties of behavioral addiction[87].

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