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Association of Pre-existing Mental Health Conditions with Acute Mountain Sickness at Everest Base Camp

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Abstract

Background
Mental health disorders are common, but limited data are available regarding the number of people with a past medical history of psychiatric diagnoses going to high altitude. It is also unknown whether mental health conditions are associated with increased risk of acute mountain sickness (AMS).

Methods
We analyzed data from a previous study at Everest Base Camp. Participants self-reported their past medical histories and history of substance use and had a brief history taken by a physician. AMS was assessed using the self-reported 2018 Lake Louise AMS Score.

Results
Eighty-five participants (66 men, 19 women, age 38±9 years) were included. When questioned by a physician 28 participants reported prior diagnoses or symptoms compatible with depression (23%), anxiety disorder (6%), posttraumatic stress disorder (1%), and psychosis/psychotic experiences (9%). The prevalence of psychiatric diagnoses in the past medical history was much lower in the self-reported data (2/85) than in the group questioned by a physician (28/85).

Increased risks of AMS was associated with a past medical history of anxiety disorder (OR 22.7; 95%CI 2.3-220.6; p<0.001), depression (OR 3.6; 95%CI 1.2-11.2; p=0.022), and recreational drug use ever (OR 7.3; 95%CI 1.5-35.5; p=0.006).

Conclusions
Many people who go to HA have a past medical history of mental health conditions. These individuals have an increased risk of scoring positive for AMS on the Lake Louise Score compared to people without a history of mental health conditions.
Introduction

Psychiatric disorders have a high lifetime prevalence. Common mental health conditions, including mood, anxiety, and substance use disorders affect about 30% of the global population (Steel et al. 2014). Estimated lifetime prevalence of mental disorders is 29% for anxiety disorders; 21% for mood disorders; 25% for disorders of impulse control; and 15% for substance use disorders. The prevalence of any disorder is 46% showing how common mental health disorders are in the general population (Kessler et al. 2005). Although the number of people going to high altitude (HA) for work or recreation has increased steadily in recent years, little is known about HA travel in people with a past medical history of psychiatric conditions (Hüfner et al. 2019). The US Center for Disease Control (CDC) states that psychiatric conditions pose a low risk when going to HA (CDC 2019). However, there is an almost complete lack of scientific studies. It is not known how many people with mental health problems travel to HA and whether they are more susceptible to acute mountain sickness (AMS) or sleep impairment than people without mental health problems. It is also not known whether AMS symptoms or sleep impairment at altitude can worsen psychiatric symptoms or lead to recurrences of dormant psychiatric conditions. Complicating the situation, symptoms of AMS and mental health disorders, such as anxiety, can be similar (Boos et al. 2018; Dong et al. 2013). It is possible that symptoms of pre-existing psychiatric diagnoses and AMS symptoms overlap, obscuring the diagnosis. More data is needed on which to base advice for people with mental health problems traveling to HA regarding preparation, potential medication changes, and awareness of new or worsening symptoms.
Our goal was to investigate the prevalence of pre-existing psychiatric diagnoses or symptoms compatible with a mental health disorder in individuals traveling to high altitude and to evaluate the association with current AMS symptoms.

Methods
Study setting
The data were collected as part of a previous study at Everest Base Camp (EBC) and represent a secondary analysis (Hüfner et al. 2021). Data were collected by author F.C., a physician from South Tyrol, Italy without speciality training at the time, who received training in psychiatric diagnostics (MINI interview and diagnostic criteria of major psychiatric disorders) prior to the study by K.H, a board-certified neurologist, psychiatrist, and specialist in psychotherapeutic medicine. The study took place during April and May 2019 at EBC (5365 m). Questionnaires were completed digitally on a tablet.

Participants
Climbers and accompanying staff with adequate command of the English language were included in the previous study. Since climbers participated in multiple phases during acclimatization climbs (“rotations”), there were multiple sets of data for each climber. The study was approved by the Nepal Health Research Council. Informed written consent was obtained from each participant prior to inclusion in the study.

Questionnaires and clinical examination
We established the questions based on the Strengthening Altitude Research (STAR) data-reporting guidelines for clinical high altitude research (Brodmann Maeder et al. 2018). We
analyzed participant self-rated answers to questions regarding demographic and social data, including lifestyle habits and substance use. Questions addressed alcohol consumption and recreational drug use prior to and during the expedition. There were open-ended questions about past medical history, the 2018 Lake Louise AMS score (LLS) (Roach et al. 2018), and problems sleeping. The observer-based ratings were the Mini International Neuropsychiatric Interview English Version 7.0.1 for DSM-5 (M.I.N.I. psychosis module) (American Psychiatric Association 2013; Sheehan et al. 1998) and open-ended questions about previous psychiatric symptoms and conditions. A psychiatric diagnosis was assumed by the observer when individuals reported symptoms compatible with a psychiatric disorder according to standard diagnostic criteria (American Psychiatric Association 2013). These criteria do not classify normal fear when facing a challenging task as an anxiety disorder. Single specific phobias such as arachnophobia that did not affect daily functioning were not assessed. AMS was diagnosed according to the LLS 2018 guidelines. A diagnosis of AMS required a total score ≥3 with at least 1 point for headache (Roach et al. 2018). The AMS clinical functional score was also collected.

Statistical Analysis

Individual data sets were collapsed for each participant: Individuals were scored as AMS positive if they reported AMS according to the LLS 2018 guidelines in at least one of the collected questionnaires. They were scored as positive for a single AMS symptom such as headache or fatigue if they had reported the symptom on at least one of the questionnaires. A history of a psychiatric disorder was only assessed once, so that it was not necessary to collapse these data. We present the data as absolute numbers, mean, standard deviation, and percentages. We calculated odds ratios (OR) from the 4x4 tables. We used the Chi-Square test to compare binary data and the Mann-Whitney U test for numeric data. P<0.05 (2-sided) was considered significant.
We analyzed the data using IBM SPSS Statistics Version 25 (IBM Corporation, Armonk, NY, USA).

Results

Ninety-nine climbers and accompanying staff were included in the original study. Two participants were excluded during the primary analysis, one because of internally inconsistent data and the other because of a brain lesion that may have invalidated the data for that participant. The data sets of 12 additional participants were excluded because they had been collected in a pilot study the previous year and contained no data on psychiatric conditions. Ultimately, we analyzed data from 85 participants (66 men, 19 women, Table 1).

When questioned directly by the physician 10/85 (12%) reported a past medical history of a mental health disorder, that had been diagnosed or treated specifically by a mental health professional and 18/85 (21%) reported a past medical history of signs and symptoms compatible with a mental health disorder but had not received treatment or a formal diagnosis (Table 2). Nine of the 85 (11%) participants reported more than 1 psychiatric diagnosis. The reported conditions were depression, anxiety disorder, posttraumatic stress disorder (PTSD), and psychosis. One participant reported treatment with sertraline during the expedition. Only 2 of the 85 (2%) participants self-reported a previous psychiatric diagnosis. These individuals also reported a diagnosis of a mental health condition when questioned by a physician. Sociodemographic characteristics and factors related to the climb were compared between the groups with and without a past medical history of a mental disorder (Table 1). The mean age was 39±10 years in the group without a history of a mental disorder and 36±7 years in the group with a past medical history of a mental disorder (Mann Whitney U Test, Z -0.861, p = 0.389).
Sixteen of the 85 (19%) individuals fulfilled Lake Louise AMS criteria at least once over the course of the study. There were increased risks of AMS with anxiety disorder (OR 22.7; 95%CI 2.3-221; p<0.001, limited validity of the statistical calculations due to the low number of individuals with a history of anxiety disorder without AMS), depression (OR 3.6; 95%CI 1.2-11.2; p=0.022), and recreational drug use ever (OR 7.3; 95%CI 1.5-35.5; p=0.006) (Table 3 and supplemental material).

In subjects with depression and anxiety disorder in their past medical history, the LLS symptom “fatigue” showed the highest OR. Individuals with a past medical history of a psychiatric condition showed higher clinical functional AMS scores ($\chi^2$ 5.94 df 2, p=0.051, 3 missing data).

There was no increased risk of sleep disturbance in participants with a past medical history of psychiatric diagnoses with 5/28 (18%) showing sleep disturbances at altitude compared 8/57 (14%) individuals without a history of psychiatric diagnoses ($\chi^2$ 0.21, df 1, p=0.645; Table 1).

**Discussion**

A significant proportion of individuals interviewed at EBC reported psychiatric symptoms compatible with a past medical history of psychiatric diagnosis or had previously been diagnosed with a mental health disorder by a professional. The lower prevalence of psychiatric diagnoses in self-reported data compared to data collected by a physician probably reflects the stigma associated with mental health issues (Corrigan and Watson 2002) and the need for direct questioning in order not to miss relevant information. Lower prevalence of self-reported psychiatric diagnoses could also be influenced by other factors related to demographics or cultural influences, or could simply be caused by recall bias. The numbers of participants
reporting previous psychiatric diagnoses seems consistent with general population-based data for
depression (Kessler et al. 2005). The prevalence of anxiety disorders was lower than expected,
possibly because participants with anxiety are less likely to engage in activities they perceive as
potentially dangerous (Grupe and Nitschke 2013). The number for history of psychosis was
higher than would be expected for genuine psychotic disorders such as schizophrenia or
depression with psychotic symptoms, probably because also externally triggered episodes such as
by exhaustion, which should probably better be classified as psychotic experiences i.e. episodes
in the absence of a mental illness were classified here (Hinterbuchinger et al. 2021, Pignon et al.
2018). Many mountaineers use legal or illegal substances to enhance their performance (Robach
et al. 2016). One participant reported being treated with sertraline during the expedition. Animal
models suggest that some antidepressants might not be as effective at HA as at sea level (Kanekar
et al. 2018). High risk sports can be used by individuals with alexithymia i.e. with problems in
recognizing and expressing ones emotions to experience emotions (Barlow et al. 2015) but can
also be used for emotional regulation (Barlow et al. 2013). Both uses may be important in
psychiatric disorders such as depression (Ehring et al. 2008; Honkalampi et al. 2000).

The observed association of depression and anxiety disorders with higher OR for AMS could be a
sign of a common underlying mechanism such as a shared underlying genetic or epigenetic
vulnerability. Genetic factors have been described for disorders such as depression and anxiety
(Shadrina et al. 2018), as well as for AMS (Rupert and Koehle 2006). It is more likely that
participants with anxiety or depressive disorders show an increased awareness of somatic
symptoms. High levels of anxiety before HA exposure are associated with higher levels of
anxiety at high altitude and a higher incidence of AMS (Boos et al. 2018; Missoum et al. 1992)
and HA headache (Bian et al. 2013). Improved sleep at HA, using temazepam, a drug that may
also alleviate symptoms of anxiety and partly depression, was not associated with improvements in AMS scores (Tanner et al. 2013). Increased mental stress at HA in individuals with prior diagnoses of mental disorders could mediate the associations between pre-existing mental health disorders and AMS via physiological responses such as the cortisol pathway, the sympathomedullary pathway or low-grade information i.e. a subclinical syndrome of elevated inflammatory markers (Burtscher et al. 2022; Gatterer et al. 2019; Schneiderman et al. 2005).

Higher somatization scores at sea level are a predictor of AMS (Bian et al. 2016). Most studies that have investigated anxiety or somatization used healthy participants who did not have mental health disorders. Another possible explanation might be that an increased LLS does not reflect increased HA-related somatic symptoms, but rather deterioration of a pre-existing mental condition. Symptoms such as nausea, dizziness, and weakness are also found in anxiety and depressive disorders. HA with associated alterations in sleep patterns may be a risk factor for worsening or relapse of psychiatric disorders (Hüfner et al. 2019). In a field study with 18 participants AMS symptom burden throughout the trek was found to cluster with sea level measures of anxiety, agoraphobia, and neuroticism rather than oxygen saturations. The authors concluded that the contribution of psychological factors to individual experiences of AMS symptoms should be studied in more detail in the future (Talks et al. 2022).

There is a possibility that pre-existing disorders may confound the LLS (Woolcott 2021), since many of the AMS symptoms are identical to symptoms experienced by common mental disorders such as depression or anxiety disorders. Changes in neurotransmitter dynamics at HA caused by hypoxia, cold, or other stressors or by changes in steady state plasma levels of psychiatric medications might lead to exacerbation of psychiatric symptoms (Arancibia et al. 2003; Institute
of Medicine (US) Committee on Military Nutrition Research 1996). Individuals affected by AMS tend to have more negative moods than those who feel well (Crowley et al. 1992), consistent with these possible associations.

Symptoms of anxiety or anxiety disorders can occur for the first time at altitude and can be related to various physiological factors such as hyperventilation, periodic breathing or problems with sleep, but also to environmental or cultural variations (Fagenholz et al. 2007). Also, psychological factors such as being in a location far from home or in a remote area where medical care is not immediately at hand can also provoke symptoms of anxiety that exceed realistic fears. Anxiety might also occur at altitude by chance, since anxiety disorders are among the most common psychiatric problems. Anxiety can be so severe that evacuation is warranted from high altitude (Basnyat and Litch 1997).

**Limitations**

Differences in the ability to acclimatize to HA might be present in individuals with and without histories of a mental health disorders. This might affect the observed associations. Also, our results may not be generalizable to individuals in various situations, such as working in HA mining. Regular alcohol consumption prior to the expedition and prevalence of prior recreational drug use were likely overestimated in our survey, because we did not specifically assess diagnostic criteria for abuse or dependency (American Psychiatric Association 2013) and also for the other psychiatric conditions (except psychosis/psychotic experiences) we could not demonstrate whether the symptoms and severity of specific conditions met internationally recognized diagnostic criteria, because we did not use a standardized assessment tool. The validity of more elaborate statistical models such as regression analyses was not given due to
small sizes of individual subgroups (e.g. only one individual with a history of an anxiety disorder
did not score AMS positive, supplemental material). Unfortunately, we did not systematically
record whether the reported mental health conditions were active at the time of HA exposure or
immediately prior to the HA exposure or whether symptoms relapsed during HA exposure.

Conclusions
Many people who go to HA have a past medical history of mental health conditions. When
directly questioned by a physician, about one-third of a convenience sample of participants on
HA expeditions at EBC reported having a past medical history of psychiatric diagnoses or
symptoms compatible with psychiatric diagnoses. Medical personnel on expeditions should
inquire specifically about mental health disorders and should not expect that self-report forms
will have complete information in case of an emergency.

Participants with a past medical history of psychiatric diagnoses or of symptoms compatible with
psychiatric diagnoses had an increased risk of scoring positive on the Lake Louise Score for
AMS assessment compared to participants without mental health conditions. There are several
possible mechanisms, which might account for this, related to cultural, genetic or environmental
factors. Further investigation should be undertaken to determine whether the increase in AMS
rate in individuals with a past medical history of mental health condition is related to
confounding effects of psychiatric symptoms on the LLS in these participants.

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Authorship confirmation statement

Design of study: KH, FC, AES, PFP, BB, MBM, BS-U, HB
Data acquisition: FC, SSB
Data analysis: KH, FC, AES, ERPN
Data interpretation: all authors
Writing of manuscript: KH, ERPN, KZ
Revision of manuscript for important intellectual content: all authors

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References


Table Captions

Table 1

Sociodemographic characteristics of the study population and factors related to HA. No PSY/Yes PSY indicates the groups with or without a past medical history of psychiatric conditions or symptoms compatible with such conditions. The Chi Square test was used to evaluate differences between the groups.

Abbreviations

AMS: acute mountain sickness
HACE: high altitude cerebral edema
HAPE: high altitude pulmonary edema

Table 2. Frequencies of psychiatric conditions in the past medical history and substance use behavior prior to or during HA exposure

Frequencies are given as participants with positive answers/all participants with answers and as percentages. Professional diagnosis indicates that the individual had been diagnosed by a mental health professional. Nine individuals were affected by more than 1 mental health disorder

PTSD: posttraumatic stress disorder

n.a.: not applicable

* limited validity of the statistical calculations due to the low number of individuals with a history of anxiety disorders who did not develop AMS, see also supplemental material

Table 3. Associations of psychiatric conditions and substance use behavior prior to HA exposure with AMS LLS Scoring

Odds ratios (OR) and 95% confidence intervals (CI) are reported.
For conditions with significantly increased ORs for AMS, individual LLS symptoms were analyzed and significant differences are indicated. This calculation also includes individuals with single symptoms of AMS not meeting the threshold for AMS diagnosis.

P-values and test statistics are based on Chi-Square analysis.

AMS: acute mountain sickness
PTSD: posttraumatic stress disorders
LLS: Lake Louise Score
n.a.: not applicable