



Going to Altitude with a Preexisting Psychiatric Condition

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Abstract

Hüfner, Katharina, Barbara Sperner-Unterweger, and Hermann Brugger. Going to altitude with a preexisting psychiatric condition. *High Alt Med Biol.* 20:207–214, 2019.—Psychiatric disorders have a high lifetime prevalence affecting about 30% of the global population. Not much is known about high altitude (HA) sojourns in individuals living with a psychiatric condition. This lack of scientific evidence contrasts with the anticipated increase in numbers of individuals with preexisting psychiatric conditions seeking medical advice on HA exposure. Not only are there risks associated with a HA climb, but physical activity in general is known to improve symptoms of many psychiatric disorder and enhance measures of mental well-being like quality of life and resilience. There are additional positive effects of alpine environments on mental health beyond those of physical activity. All individuals going to HA with a preexisting psychiatric condition should be in a state of stable disease with no recent change in medication. Specific considerations and recommendations apply to individual psychiatric disorders. During the HA sojourn the challenge is to separate altitude-related symptoms such as insomnia from prodromal symptoms of the underlying disorder (e.g., depressive episode) or altitude-related hyperventilation from panic attacks. In case an individual with preexisting anxiety disorder decides to go to HA there might be a predisposition toward acute mountain sickness (AMS), but it should always be considered that many symptoms of anxiety and AMS overlap. Any medication that is anticipated to be taken during ascent or at HA should be tested for compatibility with the psychiatric condition and medication before the trip.

Keywords: clinical guideline; high altitude; mood disorder; psychiatric disorders; psychiatric medication

Introduction

PSYCHIATRIC DISORDERS have a high lifetime prevalence, with common mental disorders (anxiety, mood, and substance disorders) affecting ~30% of the global population (Steel et al., 2014). Not much is known about high altitude (HA) sojourns [defined as sojourns >1500 m (Roach

et al., 2017)] in individuals living with a psychiatric condition. This lack of information and evidence might partly stem from the fact that the lower socioeconomic status associated with psychiatric conditions may prevent travel to HA for leisure purposes (Mangalore et al., 2007). In addition, there is still a stigma associated with admitting to having “mental health problems,” so that individuals affected by a psychi-

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atric condition might have travelled to HA without informing anyone of their underlying condition.

Due to the scarcity of information on the topic of travel to HA with a preexisting psychiatric condition, we infer most information and recommendations in this article from studies performed at sea level or from theoretical considerations. Nothing is known about which altitudes and which duration of exposure to HA is critical for individuals with preexisting psychiatric disorders. On a pathophysiological basis, changes in neurotransmitter utilization and concentration at HA, induced by hypoxia, cold, or other stressors could be important (Institute of Medicine [US] Committee on Military Nutrition Research, 1996; Arancibia et al., 2003) and changes in plasma levels of permanent psychiatric medications can lead to exacerbation of psychiatric symptoms.

In this short clinical summary we try to provide guidance for medical personal who is advising individuals with a preexisting psychiatric condition on their fitness to travel to HA. We encourage discussion on these probably under-reported disorders in the context of HA and would very much welcome the reports of individuals with mental disorders or doctors who have experience in taking individuals with preexisting psychiatric conditions to HA. The occurrence and treatment of psychiatric conditions in long-term HA residents and newly occurring HA-induced psychiatric disorders are not covered here.

General Recommendations

Although a few hours trip to altitudes ~ 3500 m using vehicles or cable cars for ascent probably only has few restrictions, any exposure ~ 5500 m [extreme altitude (Roach et al., 2017)] and for longer durations or in more remote areas should always be carefully and thoroughly planned weighting risks and benefits. Taking someone with a stable preexisting psychiatric condition, that is, symptom free or with minor residual symptoms for at least 6 months (van Os et al., 2006) to HA, should be weighted and evaluated in a similar way as it would be carried out for someone with a stable cardiac or respiratory condition. To be able to perform such an evaluation clinical experience and theoretical background knowledge of the most common psychiatric disorders is essential.

For the accompanying doctor and the afflicted individual knowledge about possible emergency and evacuation scenarios is crucial. The members of the climbing/expedition team or at least the tent mate and the accompanying medical personnel should be informed about the individuals' condition and which symptoms to watch for that might hint toward aggravation or exacerbation of the condition. One of the challenges will be to separate altitude-related symptoms such as insomnia from prodromal symptoms of the underlying disorder (e.g., depressive episode) or altitude-related hyperventilation from panic attacks. Any medication that is anticipated to be taken during ascent or at HA (e.g., acetazolamide and sleep medication) should be tested for compatibility with the psychiatric condition and medication before the trip.

Positive Effects of Taking Individuals with Psychiatric Conditions to Altitude

Not only are there risks associated with a HA climb, but physical activity in general is known to improve symptoms of depression, anxiety, and panic disorder (Strohle, 2018) and

enhance measures of mental well-being like quality of life (Svantesson et al., 2015) and resilience (Ho et al., 2015). There is a positive effect of physical activity in an alpine environment on mental health beyond that of physical activity itself (Ower et al., 2018). By building a personal bond to individual mountain sides the positive impact of the outdoor environment on mental well-being is enhanced (Knez and Eliasson, 2017). A mountain hiking program in the Alps has been shown to improve hopelessness, depression, and suicide ideation in patients suffering from high-level suicide risk (Sturm et al., 2012).

Mood Disorders

Mood disorders comprise the diagnostic categories of unipolar depressive or bipolar disorder. Depressive symptoms can be triggered by exposure to HA as has been found in chamber and field studies on healthy volunteers (Shukitt-Hale et al., 1998; Li et al., 2000; de Aquino Lemos et al., 2012; Ahmad and Hussain, 2017). One case report exists about the occurrence of mania at HA in a patient with a prediagnosed bipolar disorder (Brahm and Puls, 2011). It is unknown, however, if the risk of developing mood symptoms at HA is increased in individuals with a prediagnosed mood disorder. Suicidality is more common in people who live at altitude than in those living at sea level, but nothing is known about short-term stays (Reno et al., 2018).

Several factors can negatively influence a preexisting mood disorder at HA: (1) Disturbances in the sleep-wake cycle at HA (Tanner et al., 2013) can precipitate mood changes and acute episodes of a mood disorder (Perlman et al., 2006) more so in women than men (Saunders et al., 2015). On the contrary, sleep disturbance can be a prodromal symptom of bipolar and possibly also unipolar episodes (Jackson et al., 2003). (2) Physical, psychological, environmental, and other stress factors can occur during expeditions to HA and are linked to recurrence of mood disorders (Hammen, 2016). (3) Rigorous training in challenging environments may result in enduring negative moods (Bardwell et al., 2005). (4) Individuals affected by acute mountain sickness (AMS) tend to have more negative moods than those who feel well (Crowley et al., 1992).

Pathophysiological links connecting mood changes and HA could be the increased cortisol levels (Park et al., 2014) and low-grade inflammatory responses (Al-Hashem et al., 2014; data from rats). Serotonin (one of the key mediators of depression) is reduced at altitude in animal models (Prioux-Guyonneau et al., 1982). Selective serotonin reuptake inhibitors which are used for acute treatment and as a prophylaxis in individuals remitted from an acute depressive episode, were largely ineffective in hypobaric hypoxia in an animal model (except sertraline), possibly because of a hypoxia-induced serotonin deficit (Kanekar et al., 2018).

It can be assumed that individuals with a stable mood disorder can travel to HA without excessive risk of deterioration (authors' expert opinion). Vigilance is necessary to detect prodromal signs of mood alteration early in the course. Individuals diagnosed with a bipolar disorder with rapid cycling (at least four episodes of the bipolar disorder in the past 12 months) should be advised cautiously about going to HA as should individuals who have previously experienced very severe episodes of a mood disorder accompanied by risk to self or others (authors' expert opinion). When treating

insomnia one should keep in mind the preexisting medication not to oversedeate the individual (see Psychiatric Medications and Interactions-Important Considerations before HA Exposure) (Table 1).

Schizophrenia and Related Disorders

Psychosis is a hallmark of schizophrenia but also occurs in mood disorders, substance abuse, or delirium. HA in itself can trigger symptoms of psychosis such as “isolated psychosis” (Hufner et al., 2018); however, there is no information available if such symptoms at altitude are more likely to occur in individuals with preexisting psychotic disorders such as schizophrenia. For individuals living with schizophrenia who aim to go to altitude, clinical advice seems similar to what has been outlined for mood disorders previously. As a rule, if an individual with schizophrenia is stable and has a good insight into prodromal symptoms of recurring episodes and the disease in general, this should not preclude travel to HA (authors’ expert opinion). However, sleep disturbances should be observed and handled with care: as for mood disorders this can be a preceding sign for an acute psychotic episode (Yung and McGorry, 1996) or in itself aggravate psychotic symptoms (Freeman et al., 2009). When treating insomnia one should keep in mind the preexisting medication not to oversedeate the individual (see Psychiatric Medications and Interactions-Important Considerations before HA Exposure) (Table 1).

Anxiety

Anxiety is a life-sustaining physiological reaction to cope adequately with difficult and/or dangerous situations. However, anxiety and fear are part of various psychiatric disorders like major depression, acute psychosis, stress and trauma-related disorders, and specific anxiety syndromes, such as panic disorder. Many individuals with severe, preexisting anxiety disorders will not attempt to go to HA because of the nature of their disease. For individuals with a preexisting anxiety disorder there is probably a predisposition toward AMS at HA (Boos et al., 2018); however, most studies also included individuals with subclinical anxiety syndromes that limits transfer to a clinically ill population.

Studies have shown anxiety at HA to correlate with the severity of insomnia and tachycardia (Dong et al., 2013), and high levels of anxiety before HA exposure were associated with higher anxiety during the climb, higher levels of AMS (Missoum et al., 1992; Boos et al., 2018), and HA headache (Bian et al., 2013). Of 1036 subjects studied, 7 developed anxiety symptoms in the first days after transfer to a HA of which 4 subjects had previous diagnosis of anxiety, depression, or post-traumatic stress disorder (PTSD), so that possibly these preexisting diagnoses confer a risk factor (Sracic et al., 2014).

Individuals exposed to HA often experience somatic symptoms triggered by hypoxia, such as breathlessness, palpitations, dizziness, headache, and insomnia. Most of these symptoms are identical to those reported in panic attacks or severe anxiety (Roth et al., 2002). There are individual reports of patients with diagnosed anxiety disorder experiencing severe panic attacks at HA (Roth et al., 2002).

Hyperventilation, which often occurs at altitude, also induces panic attacks (Kinkead et al., 2014), and might be one

of the mechanisms by which HA induces symptoms of panic and anxiety (Roth et al., 2002). Whether the increase in ventilation (tidal volume) induced by acetazolamide at HA (Leaf and Goldfarb, 2007) induces panic attacks is currently not known. Acetazolamide reduces periodic breathing during the night thereby improving sleep quality (Liu et al., 2017), which might help to reduce the risk for nocturnal panic attacks when given prophylactically. Having a patient with a panic attack breathe into and out of a paper bag, an emergency measure often used at lower altitudes, can induce hypoxemia at extreme HA. At HA anxiety symptoms can lead to dangerous situations by causing feelings of dizziness or derealization, or by making it difficult if not impossible to separate them from AMS or other somatic disorders. Individuals should be counseled about this point and be advised about the similarity of AMS symptoms and symptoms of anxiety.

Post-Traumatic Stress Disorder

PTSD can develop after mountain- and altitude-related traumatic events such as avalanches or falls with subsequent injury to oneself or team mates (Peck et al., 1996) or can be related to the disadvantageous living conditions found in some parts of the world. Symptoms of PTSD include negative mood, dissociative symptoms, an altered sense of reality, or hyperarousal symptoms like sleep disturbance and problems with concentration. It is obvious that such symptoms can lead to detrimental situations at altitude. Re-exposure to a traumatic stimulus at altitude (e.g., previous accident on the same mountain) can aggravate symptoms of ongoing PTSD (Schock et al., 2010).

We thus discourage individuals with manifest PTSD to go on expeditions or to HA (authors’ expert opinion) unless this is part of a controlled, therapeutic exposure setting. Individuals who previously suffered from PTSD or who had previously been traumatized without developing PTSD are more vulnerable to increased PTSD symptoms after re-traumatization by experiencing a new traumatic event (Kinzie et al., 2002; Schock et al., 2016). Individuals with previous trauma experience need to be informed about this before the climb.

Substance Use Disorders

Substance use disorders are very common in the general population with the most common being alcohol, benzodiazepines, and cannabis, and it is known that many mountaineers use legal or illegal substances to enhance their performance (Roggla et al., 1993; Robach et al., 2016). Smoking is more common in individuals with psychiatric disorders (Boksa, 2017), and one study has shown that it might reduce the risk of AMS during acute exposure to an altitude of 3700 m (Song et al., 2014). Practical experience has shown that many individuals reduce cigarette consumption when on expeditions at HA, which can alter medication plasma levels (see Psychiatric Medications and Interactions-Important Considerations before HA Exposure) (Table 1).

Substance use should be directly asked for when evaluating an individual for their fitness to go to HA. Individuals with an ongoing substance use disorder (other than cigarette consumption) should not travel to HA, because there are risks associated with the use of substances (e.g., oversedation) and with their discontinuation (e.g., seizures and withdrawal syndromes) (authors’ expert opinion). For individuals who have overcome a substance use disorder this does not pre-

TABLE 1. PSYCHIATRIC MEDICATIONS AND INTERACTIONS — IMPORTANT CONSIDERATIONS BEFORE HIGH-ALTITUDE EXPOSURE

<i>Substance class</i>	<i>Used primarily for^a</i>	<i>Selected side effects/problems with special significance at HA^b</i>	<i>Assumed drug safety at HA</i>
			<i>Safe Caution Avoid</i>
Reuptake inhibitors (SSRI, SNRI, NDRI)	Antidepressant, anxiolytic used in long-term treatment	CYP 1A2 interaction: concentrations of fluvoxamine and duloxetine increase with reduced smoking (Oliveira et al., 2017) Reduced efficacy of mechanism of action (serotonin increase) (Kanekar et al., 2018) Serotonergic syndrome can occur in combination with some opioids such as tramadol, MAO inhibitors such as moclobemide or linezolid (Gillman, 2005) QTc prolongation especially in citalopram and escitalopram (Beach et al., 2018) Do not suddenly discontinue (discontinuation syndrome)	×
Mirtazapine, trazodone	Antidepressant, anxiolytic used in long-term treatment	CYP 1A2 interaction: concentrations of mirtazapine and trazodone increase with reduced smoking (Oliveira et al., 2017) Sedation with next day neurocognitive or motor impairment	×
Tricyclic antidepressants	Antidepressant, anxiolytic used in long-term treatment	Do not suddenly discontinue (discontinuation syndrome) Anticholinergic side effects can lead to confusion, raised intraocular pressure, or urinary retention. Intraocular pressure is already increased in individuals with acute altitude exposure (Sommer et al., 2007) Sedation with next day neurocognitive or motor impairment is especially important in amitriptyline, doxepin, imipramine, and trimipramine	×
MAO inhibitor (moclobemide, tranylcypromine)	Antidepressant, anxiolytic used in long-term treatment	Tranylcypromine is an irreversible MAO inhibitor with a very high risk for interactions with medications and foods Interactions with all serotonergic medications, also for example, opioids such as tramadol or carbamazepine (Gillman, 2005) Blood pressure variations	×
First generation, sedating antipsychotics (e.g., levomepromazine, chlorprothixene)	Antipsychotic treatment, psychomotor agitation	Do not suddenly discontinue (discontinuation syndrome) Anticholinergic side effects can lead to confusion, raised intraocular pressure or urinary retention. Intraocular pressure is already increased in individuals with acute altitude exposure (Sommer et al., 2007)	×
Clozapine, olanzapine	Antipsychotic treatment, mood stabilizer	Sedation with next day neurocognitive or motor impairment CYP 1A2 interaction: concentrations of clozapine and olanzapine increase with reduced smoking (Sagud et al., 2009) Anticholinergic side effects can lead to confusion, raised intraocular pressure, or urinary retention. Intraocular pressure is already increased in individuals with acute altitude exposure (Sommer et al., 2007) Sedation with next day neurocognitive or motor impairment	×
First and second generation nonsedating antipsychotics (e.g., haloperidol, amisulpride, risperidone)	Antipsychotic treatment, mood stabilizer	Hypersalivation especially with clozapine Possible respiratory depression especially in combination with benzodiazepines CYP 1A2 interaction: concentrations of fluphenazine and haloperidol increase with reduced smoking (Sagud et al., 2009) Increased risk for dyskinesia when combined with for example, metoclopramide QTc prolongation especially with haloperidol, ziprasidone, and iloperidone (Beach et al., 2018)	×

(continued)

TABLE 1. (CONTINUED)

Substance class	Used primarily for ^a	Selected side effects/problems with special significance at HA ^b	Assumed drug safety at HA	
			Safe	Caution Avoid
Lithium	Mood stabilizer	Narrow therapeutic range Serum levels can be changed by changes in electrolyte levels, diuretic treatment, and hematocrit (Arancibia et al., 2003). Interaction with medications commonly used at altitude such as acetazolamide and tetraacyclines (McGennis, 1978) and NSAID Carbonic anhydrase inhibitor activity, ~25% that of acetazolamide that could be beneficial at altitude (Maa, 2011). Cognitive side effects Multiple side effects (anticholinergic, serotonergic) High potential for interactions with other medications (especially Warfarin) Side effects most commonly during initial titration phase (ataxia, insomnia, headache, and rash) Sedation with next day neurocognitive or motor impairment Increased risk for hemorrhage Sedation with next day neurocognitive or motor impairment Respiratory depression Temazepam has best evidence for use at altitude (Luks, 2008) Sedation with next day neurocognitive or motor impairment Respiratory depression Zolpidem and zaleplon have best evidence for use at altitude (Luks, 2008)	×	×
Topiramate	Different off-label uses in psychiatric patients		×	
Carbamazepine	Mood stabilizer			×
Lamotrigine	Mood stabilizer		×	
Valproic acid	Mood stabilizer			×
Benzodiazepines	Sedative, anxiolytic		×	
Z substances	Sedative		×	

This table includes possible problems that can occur when using psychiatric medications at altitude; this is not a general listing of side effects of the respective medication. This table is not all inclusive and contains subjective weighting of the authors. Please refer to medication prescribing information for details.

^aPlease note that this indicates general mechanisms of action and not approved indications, which can vary between specific agents and countries.

^bSide effects outlined in the prescribing information of the drug are not referenced.

HA, high altitude; MAO, monoamine oxidase inhibitor; NARI, noradrenaline reuptake inhibitor; NDRI, noradrenaline dopamine reuptake inhibitor; NSAID, nonsteroidal anti-inflammatory drug; SSRI, serotonin noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

clude any expeditions to HA; however, it is advisable to inform the accompanying physician because benzodiazepines or Z-drugs (nonbenzodiazepine drugs with mainly hypnotic effects such as Zolpidem) should be avoided (authors' expert opinion).

Somatic Symptom Disorder

Somatic symptom disorders, also known as somatoform disorders, are physical symptoms that point toward an illness or injury, but which cannot be explained fully by a general medical condition or by the direct effect of a substance (American Psychiatric Association, 2013). Individuals with a somatic symptom disorder are usually too worried about their health and tend to avoid to put any stress on their bodies so that they will usually not attempt to go to HA. In case individuals with a somatic symptom disorder plan to travel to HA it is important to inform them about possible somatic symptoms occurring because of HA exposure, which they will experience and that they will probably be more worried about them: higher somatization score at sea level was found to be a predictor of AMS (Bian et al., 2016).

Neurocognitive Disorders

At present the record of summiting Everest is held by 80-year-old Yuichiro Miura, Japan (The Guardian, 2017). With older people going to HA beginning neurocognitive impairment can be unmasked at HA. This is pathophysiologically related to changes in acetylcholine metabolism occurring at HA also in previously healthy individuals (Institute of Medicine [US] Committee on Military Nutrition Research, 1996). Preexisting dementia or neurocognitive impairment is one of the most important risk factors for developing delirium at sea level and probably also at HA (Ahmed et al., 2014).

Delirium is a strong risk factor for subsequent dementia in older individuals (Davis et al., 2012). Individuals with insipient or manifest neurocognitive impairment before the climb should not be advised to go to HA because the exacerbation at HA can lead to dangerous decisions (authors' expert opinion). It might thus be helpful to perform a brief neuropsychological screening before going to HA in individuals where a beginning neurocognitive decline could be suspected.

Personality Disorders

One of the diagnostic criteria of personality disorder (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, DSM-5) is impairment in self or interpersonal functioning (American Psychiatric Association, 2013). Obviously, this can lead to problems in any HA expedition in which team spirit and team behavior are essential. Several studies have investigated the personality traits of mountaineers using different models of "personality" but no tightly defined personality profile among mountaineers was found (Ryn, 1988; Nicolas et al., 1999). It remains unclear whether personality disorders (as a medical condition, not personality traits) are prevalent in mountaineers (Monasterio et al., 2014). A significant association between the parameter of cooperativeness (how well adapted the individual is in getting along with others fairly and flexibly) and the total number and severity of accidents has been described (Monasterio et al., 2014).

Psychiatric Medications and Interactions— Important Considerations Before HA Exposure

Depending on the prediagnosed psychiatric condition, regular and an "emergency" medication should be carried by the individual or the accompanying doctor when going to HA. All medication that is possibly intended to be used at HA should be tested at sea level beforehand. Important medication interactions such as those with psychiatric medication and acetazolamide or antibiotics ought to be investigated beforehand.

The use of medication to improve sleep or reduce restlessness (e.g., z-drugs or benzodiazepines) maybe a bit more liberal in patients with preexisting mood or psychotic disorders to avoid aggravation of symptoms of the underlying condition owing to lack of sleep. There is the potential risk of respiratory depression (especially when combining sedating drugs such as olanzapine or mirtazapine with benzodiazepines; see medication prescribing information) and a larger risk of next day neurocognitive or motor impairment. Possibly the switch of the antipsychotic treatment to a non-sedating antipsychotic such as amisulpride before HA exposure and adaptation of the antidepressive treatment to a less sedating alternative is helpful. It is important that the process of switching medication is completed and the person is very well adapted to the new therapy prior to HA exposure.

If an individual on a sedating psychiatric medication is going to HA this person might be difficult to rouse during sleep. This could be a problem when getting up in the middle of the night for a summit attempt. It should be considered to reduce the dose of a sedating medication the evening before such an endeavor. It is important that such a "skipping" of medication only be performed once the patient is in a steady state of medication. It is also worth considering to treat a patient requiring antipsychotic therapy with a long-acting injectable to avoid problems with medication compliance and to eliminate first-pass metabolism, decreasing the potential for drug–drug interactions (Zhornitsky and Stip, 2012). It is important to mention that steroids can exacerbate psychotic and mood disorders.

Altitude medicine experts agree that in sum four medications seem to be safe and effective for improving sleep at HA: acetazolamide, temazepam, zolpidem, and zaleplon (Luks, 2008). Safe in the HA medicine context means that they do not lead to a significant respiratory depression and do not cause significant impairment the next day. For antihistamines and low-potency sedating antipsychotics (e.g., melperone) there are no studies, but they might have to be used in individuals with contraindications for benzodiazepines. The use of any kind of psychoactive drug may be subject to governmental regulations and strict customs control. This should always be considered when medications are brought in foreign countries and one crosses a border.

Limitations and Conclusion

We recognize that there is very limited scientific evidence on the subject of going to altitude with a preexisting psychiatric condition, which is covered in this practical clinical overview. Many recommendations are thus extrapolated from experience gained at lower altitude and based on expert opinion. Clinical studies are necessary to provide more robust information to patients living with psychiatric conditions and seeking our advice on HA exposure. Until these studies are available, we will have to advise as best as we can using the

existing evidence. A careful weighting of risks and benefits and appreciation of the individual patient's history is essential.

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