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1 **Isolated High Altitude Psychosis, Delirium at High Altitude, and High Altitude Cerebral**
2 **Edema: Are These Diagnoses Valid?**

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27

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38 **Abstract**

39 Psychosis is a psychopathological syndrome that can be triggered or caused by exposure to
40 high altitude (HA). Psychosis can occur alone as isolated HA psychosis or can be associated
41 with other mental and often also somatic symptoms as a feature of delirium. Psychosis can
42 also occur as a symptom of high altitude cerebral edema (HACE), a life threatening condition.
43 It is unclear how psychotic symptoms at HA should be classified into existing diagnostic
44 categories of the most widely used classification systems of mental disorders, including the
45 Diagnostic and Statistical Manual of Mental Disorders (DSM-V) and the International
46 Statistical Classification of Diseases and Related Health Problems (ICD-11). We provide a
47 diagnostic framework for classifying symptoms using the existing diagnostic categories:
48 psychotic condition due to a general medical condition, brief psychotic disorder, delirium, and
49 HACE. We also discuss the potential classification of isolated HA psychosis into those
50 categories. A valid and reproducible classification of symptoms is essential for
51 communication among professionals, ensuring that patients receive optimal treatment,
52 planning further trips to HA for individuals who have experienced psychosis at HA, and
53 advancing research in the field.

54

55 **1) Introduction**

56 Medical professionals and mountaineers are aware of somatic complications of high altitude
57 (HA) exposure, but research, clinical guidelines, and knowledge among mountaineers
58 concerning mental symptoms at HA are limited. Psychopathological changes, such as altered
59 consciousness or attention, hallucinations, and delusions can occur at HA (Wilson et al.,
60 2009;de Aquino Lemos et al., 2012;Hufner et al., 2018). These changes have most commonly
61 been linked to underlying organic processes triggered by hypoxia, but also to infections,
62 environmental conditions, or drugs. Psychogenic factors such as social isolation or mental
63 stress may also play a role. Compared to somatic symptoms, mental symptoms at high altitude
64 are underreported (Hüfner et al., 2019). However, it is critical for providing appropriate
65 treatment and prognostic recommendations, to recognize mental symptoms as accurately as
66 somatic symptoms and to classify them correctly using current diagnostic categories. In our
67 opinion, several issues, some of which are universal and others of which are specifically
68 related to HA, hinder this process (Figure 1). In this hypothesis article, we provide guidance
69 on how to classify psychotic symptoms correctly using standardized diagnostic criteria.

70

71 **2) Psychosis as a psychopathological syndrome at high altitude**

72 A syndrome is a collection of individual symptoms that commonly occur together. A
73 syndrome with a specific cause is called a disease. According to the dimensional assessment
74 of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V)
75 (American Psychiatric Association, 2013) psychosis is a psychopathological syndrome
76 characterized by symptoms of hallucinations, delusions, disorganized thought/speech,
77 abnormal psychomotor behavior, and negative symptoms, as well as impaired cognition,
78 depression, and mania. Two of the symptoms must be present for the diagnosis of psychosis,
79 with at least one of the symptoms being hallucinations, delusions, or disorganized

80 thought/speech. The definition is comparable in ICD-11, although the DSM does not
81 explicitly list impaired cognition, depression, and mania (World Health Organisation,
82 2019/2021). Hallucinations and delusions are generally considered to be the defining and
83 most prevalent features of psychosis (Horga and Abi-Dargham, 2019). Symptoms of
84 psychosis and other mental symptoms occur on a continuum with normal mental states and
85 are not binary entities. Psychotic symptoms can occur in the general population, for example,
86 the personality trait of schizotypy is associated with being prone to psychotic symptoms
87 (Allardyce et al., 2007;Smith et al., 2018). Stressful life events or mental trauma are
88 potential risk factors for psychotic symptoms in the general population. (Staines et al., 2022)
89 Physiological disturbances such as sleep deprivation or sensory deprivation can trigger
90 psychotic symptoms in healthy individuals. (Daniel and Mason, 2015;Waters et al., 2018)
91
92 Psychotic symptoms at HA have mostly been described in the lay literature, in case reports,
93 and in small case series.

94 *” I climbed to the summit in four days as a member (and doctor) of a small team of Slovenian*
95 *climbers. I had almost no acclimatization but a lot of motivation... Suddenly the hallucinated*
96 *“mountain guides” started to talk to me with very sweet and energetic advice: “Jump down*
97 *the east face and in a few seconds you will be on a flat, safe place 2000 metres lower. This*
98 *will solve all your problems.” So I was standing there, at the very edge of the east face,*
99 *prepared to jump because these voices almost convinced me that jumping down the face was*
100 *the best or only solution to my problems. I almost jumped and this would have meant death*
101 *with a 100% certainty... With coming lower, hallucinations slowly disappeared. I reached our*
102 *bivouac at 6500 metres after several hours of climbing, without hallucinations but still with*
103 *cognitive impairment.” – Iztok Tomazin, Dhaulagiri winter alpine-style ascent in December*
104 *1987; slightly adapted (Hufner et al., 2018).*

105 An analysis of the lay literature suggests that hallucinations are a very prominent feature of
106 psychosis at HA that were present in 83% of the analyzed episodes (Hufner et al., 2018). The
107 so-called third man/person syndrome is the felt presence of another person who can often also
108 be seen or heard. This was the most common hallucination, occurring in 54% of cases of
109 psychosis at HA (Hufner et al., 2018). The third man/person syndrome has mostly been
110 reported by individuals exposed to high levels of stress, often in extreme environments. Many
111 accounts have been collected in a book, *The Third Man Factor*, by John Geiger (Geiger,
112 2010) and also continue to appear in the media. For example, the climber Elisabeth Revol
113 forced to bivouac at HA on Nanga Parbat in winter, a very difficult situation, described an
114 interaction with a woman who offered her hot tea to protect her from the freezing cold in
115 return for a shoe. She suffered severe frostbite. Visual, acoustic or somesthetic hallucinations
116 can also occur at HA.

117

118 Psychotic symptoms are transdiagnostic, meaning that they are not characteristic of a single
119 disorder but can be found in various conditions. Psychosis at HA can occur in the absence of
120 other clinical features as isolated HA psychosis or be accompanied by somatic or mental
121 symptoms (Figure 2). Psychotic symptoms together with other mental symptoms commonly
122 occur in mental disorders such as schizophrenia and mood disorders, Lewy body dementia,
123 delirium, or substance abuse (Fusar-Poli et al., 2017). Foreign travel can trigger psychosis
124 through stressors such as environmental conditions, unaccustomed physical exertion, and
125 psychosocial factors, all of which can also occur in HA travel (Felkai and Kurimay, 2017).

126

127 **3) Can diagnostic categories already present in DSM V be useful to assign psychosis**
128 **at HA to a diagnostic category?**

129 We also refer to ICD-11 in case substantial differences to DSM V exist.

130

131 3.1. PSYCHOTIC DISORDER DUE TO A GENERAL MEDICAL CONDITION

132 Symptoms of psychosis, such as hallucinations or delusions, can occur as consequences of a
133 medical condition. They are then classified as psychotic disorders due to a general medical
134 condition in the DSM-V (American Psychiatric Association, 2013) (Table 1) and called
135 secondary psychotic syndromes in ICD-11 (World Health Organisation, 2019/2021). At sea
136 level and low altitudes epilepsy is recognized as the most common underlying factor of
137 psychotic disorder due to a general medical condition (Clancy et al., 2014). At high altitudes
138 HACE can be the underlying condition. HACE is a life-threatening cause of psychosis that
139 requires emergent treatment. Psychosis might be an important early warning sign of HACE,
140 however this needs further validation in clinical studies.

141

142 The category of psychotic disorder due to a general medical condition may also apply to
143 isolated HA psychosis, a syndrome that is often characterized by prominent hallucinations
144 (Table 1, criterion A). The evidence is unclear whether isolated HA psychosis is a direct
145 physiological consequence of hypoxia (Table 1, criterion B). This is likely the case, because
146 symptoms of isolated HA psychosis disappear without sequelae once an individual reaches a
147 lower altitude. (Brugger et al., 1999;Hufner et al., 2018). It is debatable whether hypoxia
148 caused by ascent to HA can be considered to be a general medical condition, although this
149 would account for the generally benign nature and reversibility of symptoms once the
150 causative condition is removed.

151

152 3.2. BRIEF PSYCHOTIC DISORDER

153 The category of brief psychotic disorder in the DSM-V (similar to an “acute and transient
154 psychotic disorder” in ICD-11) requires a duration of at least one day and is often associated
155 with a stressful life event (Table 2). Travel to HA could be considered a stressful life event.
156 Stress and exhaustion have been associated with psychotic symptoms in high-performance

157 endurance athletes (Carbone et al., 2020;Huang et al., 2021). Symptom duration in isolated
158 HA psychosis can be shorter than 24 hours (Table 2, criterion B). It is unclear whether
159 isolated HA psychosis carries a risk of recurrence or predisposes an individual to other
160 psychotic disorders as does brief psychotic disorder (Fusar-Poli et al., 2022). Based on media
161 reports, individuals who have experienced psychosis at HA return to and remain at their
162 premorbid level of functioning once they descend to lower altitudes (Table 2, criterion B).
163 While brief psychotic disorders often require the treatment with antipsychotics, this has not
164 been reported in isolated HA psychoses.

165

166 3.3 DELIRIUM

167 When psychotic symptoms occur in association with disturbances in attention and awareness
168 caused by external triggers this constitutes organic brain dysfunction (classified as “delirium”
169 in the DSM-V and ICD-11; Table 3) (American Psychiatric Association, 2013;European
170 Delirium and American Delirium, 2014;World Health Organisation, 2022). Delirium at HA
171 can occur in the context of HACE or as a result of systemic conditions such as infection or
172 dehydration (Ryn, 1971;1988;Garrido et al., 2000;Basnyat, 2002). Diagnostic criteria of
173 “delirium” are comparable between ICD-11 and the DSM-V (First et al., 2021).

174

175 In a field study of mostly well-acclimatized individuals at Everest Base Camp there was only
176 one case of delirium (Hüfner et al., 2021). This is a low incidence compared to previous
177 literature (Ryn, 1988;Hufner et al., 2018). When a diagnosis of delirium is made it is essential
178 to attempt identify the underlying pathology (Table 3, criterion E). At HA it is critical to
179 consider HACE as a possible cause. HACE is a life-threatening condition that must be treated
180 emergently by descent. Isolated HA psychosis should not be classified as delirium, because,
181 the criteria of delirium, such as changes in attention and awareness or arousal (Table 3,
182 criterion A, D), are not a characterizing feature of isolated HA psychosis. There are several

183 good assessment tools available for the diagnosis of delirium. The Confusion Assessment
184 Method (CAM) must be used with a standardized interview by a trained interviewer (Inouye
185 et al., 1990). The Delirium Observation Screening Scale (DOSS) (Schuurmans et al., 2003) is
186 a screening tool that only requires observation of patients, with no specific cognitive testing.

187

188 **4. High altitude cerebral edema**

189 While most clinicians working at HA have a personal gestalt of the symptoms of HACE, there
190 are no uniform diagnostic criteria for the psychopathology defining HACE. HACE is
191 distinguished from AMS by disturbances in consciousness that may progress to coma,
192 psychiatric changes, confusion and by ataxia (Hackett and Roach, 2004). The term “altered
193 mental status,” often used to describe the mental symptoms in HACE, is a descriptive term
194 that includes a range of psychopathological symptoms. In the original consensus report mental
195 status was defined by the following categories: no change in mental status; lethargy/lassitude,
196 disoriented/confused, stupor/semiconsciousness, coma (Hackett and Oelz, 1992). In some
197 settings mental status change is equivalent to delirium with disturbances in attention,
198 awareness, cognition, and level of consciousness (American College of Emergency
199 Physicians, 1999) (Table 3). For a diagnosis of HACE, the STAR data reporting guidelines
200 define change in mental status as disturbances of orientation (to person, place and time) or
201 somnolence/confusion/coma (Brodmann Maeder et al., 2018) (Table 4). Other guidelines
202 require drowsiness, confusion, or irritability (Gallagher and Hackett, 2021). In a study
203 focused primarily on ataxia in HACE, mental status changes consisted of disturbances in
204 consciousness (79%), lassitude (41%), apathy (36 %), drowsiness (33%), psychological
205 changes (27%), disorientation (14%), and hallucinations (3%) (Wu et al., 2006).
206 Psychological changes comprised strange or irrational behavior, emotional changes, and
207 impaired long-term or short-term memory. The psychopathological symptoms of HACE are
208 multifaceted. There are no standardized assessment tools to assess symptoms. While coma is

209 relatively easy to diagnose, judgements regarding lethargy or lassitude differ among
210 evaluators. We believe that rating the changes in consciousness, using the Glasgow Coma
211 Scale or other validated scales to assess consciousness that can be easily administered by first
212 responders and others in a pre-hospital setting without formal training, such as AVPU (alert,
213 responsive to voice, responsive to pain, or unresponsive (Alexander, 1993), would be a step
214 forward to solve this problem. Using an assessment tool for delirium could also aid in
215 diagnosis.

216

217 Evaluation of possible HACE should include a full mental status examination and not be
218 restricted to consciousness. Only then would it be possible to make a full assessment of
219 psychopathological status, which is necessary to diagnose psychiatric conditions at any
220 altitude. Manic or depressive symptoms as well as anxiety, can be triggered by HA. It is
221 unclear whether these symptoms also occur in HACE (Ryn, 1988;Shukitt-Hale et al., 1991;de
222 Aquino Lemos et al., 2012;Hufner et al., 2018). A pre-existing psychiatric condition is a risk
223 factor for developing AMS. It is unclear whether this is also the case for HACE (Hufner et al.,
224 2022).

225

226 **5) Discussion and Conclusion**

227 Diagnosis of psychotic symptoms at HA is essential for communication among professionals,
228 for ensuring patients receive optimal treatment, for planning further trips to HA for
229 individuals who have experienced psychosis at HA, and for advancing research in the field. If
230 clinical and research databases of such relatively rare, but potentially dangerous, conditions
231 are developed it will be essential to reproducibly classify symptoms into diagnostic
232 categories. There are additional factors, including legal and insurance considerations, that
233 make it important to assign psychotic symptoms to the correct diagnostic categories. For
234 people going to HA, past medical history, including psychiatric and especially psychotic

235 episodes, is important information for guides, leaders, and other assessors of risk. Different
236 diagnostic categories carry different levels of concern. The most dangerous cause of delirium
237 at HA is HACE, a life -threatening condition that requires emergent treatment. Specific
238 diagnostic criteria defining the psychopathology in HACE might help differentiate HACE
239 from other HA-associated mental disorders. There is no current diagnostic category that is a
240 perfect fit for isolated HA psychosis. Isolated HA-psychosis is attributed primarily to hypoxia
241 and is usually benign and self-limiting, resolving after descent and restoration of normoxia.
242 Isolated HA psychosis exacts a personal cost to the individual who lived through the
243 experience, as well as having prognostic and legal implications. Attribution to HA and
244 complete recovery can be reassuring in the long term and can help to reduce stigma. Further
245 research and clinical case descriptions are needed to evaluate the best diagnostic category for
246 isolated HA psychosis. It is also possible that the existing diagnostic categories do not
247 adequately describe isolated HA psychosis. Available evidence suggests the following distinct
248 features of isolated HA psychosis: a) it occurs in the context of a recent gain in altitude in an
249 individual without prior history of psychosis at sea level, b) it occurs without additional
250 psychopathology such as altered level of consciousness, or prominent changes in attention and
251 awareness (suggesting for example HACE or delirium) c) the affected individual is able to
252 descend by walking without physical assistance, and d) symptoms disappear without sequelae
253 once the individual reaches lower altitude. These criteria will require testing and validation in
254 clinical practice.

255

256

257 **Tables**

258 Table 1. Diagnostic criteria of “psychotic disorder due to a general medical condition” based
259 on the DSM-V (American Psychiatric Association, 2013).

A. Prominent hallucinations or delusions.
B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct physiological consequence of a general medical condition.
C. The disturbance is not better accounted for by another mental disorder.
D. The disturbance does not occur exclusively during the course of delirium.
E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

260

261

262

263 Table 2. Diagnostic criteria of brief psychotic disorder according to the DSM V (American
264 Psychiatric Association, 2013).

<p>A. Presence of one or more of the following symptoms. At least one of these must be (1), (2), or (3):</p> <ol style="list-style-type: none">1. delusions2. hallucinations3. disorganized speech (e.g., frequent derailment or incoherence)4. grossly disorganized or catatonic behavior
<p>B. Duration of an episode of the disturbance is at least 1 day but less than 1 month, with eventual full return to premorbid level of functioning.</p>
<p>C. The disturbance is not better explained by major depressive or bipolar disorder with psychotic features or another psychotic disorder, such as schizophrenia or catatonia, and is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication), or another medical condition.</p>

265

266

267 Table 3. DSM-V TR diagnostic criteria for delirium (American Psychiatric Association,
268 2022). *

A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) accompanied by reduced awareness of the environment.
B. The disturbance develops over a short period of time, usually hours to a few days, represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
C. An additional disturbance in cognition, including memory deficit, disorientation, language, visuospatial ability, or perception.
D. The disturbances in A and C are not better explained by a pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.
E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. caused by a drug of abuse or a medication), or exposure to a toxin, or is due to multiple etiologies

269 * diagnostic criterion A has been clarified in the text revision (TR) version of DSM V.

270

271

272 Table 4. Diagnostic criteria of HACE (Roach et al., 2018)

A) Symptoms of AMS or HAPE	A) No Symptoms of AMS or HAPE
B) Mental status change	B) Mental status change
AND/OR	AND
ataxia	ataxia
C) Onset within 24-72 hours following a gain in altitude	

273 Mental status change refers to disturbances of orientation (to person, place and time) or
 274 altered consciousness with confusion, somnolence, or coma (Brodmann Maeder et al., 2018).

275 Ataxia refers to an unsteady gait or inability to walk in a straight line heel-to-toe (tandem
 276 gait). AMS: acute mountain sickness, HACE: high altitude cerebral edema, HAPE: high
 277 altitude pulmonary edema

278

279 **Figure captions**

280 Figure 1. Diagnostic difficulties encountered in trying to identify and categorize mental
281 symptoms at high altitude (HA). Barriers specific to HA are in grey. Barriers also encountered
282 in other setting are in blue.

283

284 Figure 2. The pathway from psychotic symptoms to possible diagnostic categories (boxes).

285 Possible underlying factors or conditions at high altitude are indicated in gray.

286

287

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