Isolated generalised tonic-clonic seizure at high altitude in a young male trekker with a positive family history of seizures.

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Running Title: Case Report: Generalised tonic-clonic seizure at altitude

An 18-year-old Caucasian male was trekking to Mount Everest base-camp (EBC) in Nepal during the spring of 2011. He normally lived at sea-level in the UK and had no previous medical history. His father had experienced one generalised tonic-clonic seizure aged 32, with no subsequent epileptiform events. The subject was in the control arm of a randomised controlled research study (n=40) following a standardised ascent profile to EBC (Levett et al., 2010). Every morning he completed a Lake Louise AMS questionnaire (Roach et al. 1993) and had resting heart rate (HR), respiratory rate (RR), and peripheral oxygen saturations (SpO2) measured.

Over six days, the subject had flown from Kathmandu (1300 meters) to Lukla (2800 meters) and trekked from Lukla to Pheriche (4250 meters). During this time, he reported no symptoms of AMS, whilst other research participants did experience symptoms (number of trekkers with AMS symptoms ranged between 0-9 per day). Additionally, the subject expressed no signs of high altitude cerebral oedema (HACE), and recorded physiological variables that were similar to other study participants. At rest, on the morning of the seizure (7^{th} day of trek), SpO2 was 85%, RR was 9 breaths.min^{-1}, and HR was 55 beats.min^{-1} (vs. group means of 85%, 14 breaths.min^{-1}, and 81 beats.min^{-1} respectively). The tonic-clonic seizure occurred in the absence of any obvious acute precipitating event in the presence of doctors at the Pheriche Himalayan Rescue Association clinic (4250 meters). The seizure was managed immediately with supplemental oxygen and 1000 mls of Dextrose Saline (4%/0.9%) intravenously. The seizure lasted approximately one minute and was followed by a ten minute post-ictal phase characterised by drowsiness and confusion. Following recovery and a subsequent normal physical examination, the subject stated he had no memory of the episode, did not recall an aura prior to the event, and reported feeling previously well. He was repatriated to Kathmandu where an electroencephalogram and computed tomography of his head were both reported as ‘normal’ by attending specialists. He commenced a 10-day course of Lorazepam and returned to the UK, where cranial magnetic resonance imaging was reported as normal. He remains well 17 months post the event, and has had no subsequent seizures.

This report highlights a young male with a family history of seizures, who experienced an isolated tonic-clonic seizure whilst hypoxaemic at 4250m. There was no evidence of AMS or

HACE, and based on comparisons with his immediate trekking companions cardiorespiratory physiological responses were normal for the altitude.

Due to the limited amount of epidemiological data available, it is currently uncertain if high altitude *per se* is a trigger for epileptiform seizures. A number of anecdotal reports and small studies describe the occurrence of seizures at altitude and have suggested potential risk factors including sleep disturbance (Maa, 2010), hyperventilation (Daleau et al., 2006; Maa, 2011), and the direct effects of hypobaric hypoxia (Maa, 2011). Hypoxaemia may have lowered the seizure threshold in this individual, something with potential implications for any person with either a personal or family history of seizure activity that is considering travelling to altitude. It is also possible that the occurrence of this seizure at altitude was coincidental; the rate of unprovoked seizures in a population from London has been reported at 57 per 100,000 per year (MacDonald et al., 2000). Given this uncertainty, this case report highlights the need for more robust epidemiological data collection to identify and quantify risk factors for high altitude seizures. Only through such studies will it be possible to establish whether altitude exposure *per se* increase the frequency of seizures and thereby refine advice for travellers planning ascents to high altitude.

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