The Role of Cerebral Oedema in the Development of Acute Mountain Sickness: A MRI Study

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Target Audience

Radiologists, neurosurgeons, neurologists, and physicians with an interest in basic physiology.

Purpose

Acute mountain sickness (AMS) of varying severity can develop in individuals following rapid ascent to high altitudes with low atmospheric oxygen levels, with the potentially fatal high altitude cerebral oedema (HACE) developing at the extreme end of the spectrum. The precise mechanism by which AMS occurs is currently poorly understood. One of the proposed theories is that AMS may be due to an increase in intracranial pressure as a result of cerebral oedema[1,2]. Oedema has been noted to be particularly prominent within the corpus callosum[2]. However, the evidence for the association of cerebral oedema and AMS (especially in the less severe end of the spectrum) is sparse. In light of these observations, we aimed to study the development of cerebral oedema in response to normobaric hypoxia over a 22-hour period, and its association with AMS.

Methods

Subjects (n=12) underwent 3-T MRI scanning (GE HDxt, Milwaukee USA) at baseline (FiO_2=21%) and at 2, 4, 6, 11 and 22 hours of continuous normobaric hypoxia (FiO_2=12%, approximately equivalent to an altitude of 4,400m). Diffusion weighted images (B=0, B=1000) were acquired at each time point, from which apparent diffusion coefficient (ADC) maps were calculated to assess for oedema. Region of interest (ROI) measurements of ADC values were performed on the ADC maps in the following areas (figure 1): bilateral cerebral white matter (territories supplied by the anterior, middle and posterior cerebral arteries), bilateral cerebellar white matter and the corpus callosum (genu and splenium). The Lake Louise questionnaire was used to assess for AMS at each time point. Paired t-test was used to assess the significance of changes in the mean ADC value at each time point against the baseline. Logistic regression with a single random intercept variable for subject was used to assess the association between the ADC values and the development of AMS. Significance was set at <0.05 for all statistical tests.

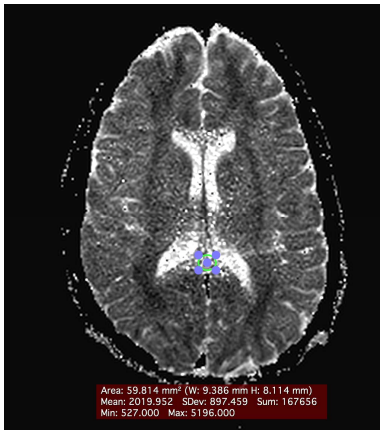

***Fig 1**: Example of an ADC map with an ROI within the splenium of the corpus callosum, giving a mean ADC value*

Results

10 subjects completed the 22-hour study and 2 subjects dropped out due to symptoms after 11 hours. 10 subjects (including the 2 subjects who retired early) developed symptoms associated with AMS by 22 hours (Lake Louise scores ≥ 3). The trends observed within the splenium and genu of the corpus callosum are displayed in figures 2 and 3, respectively. Compared to the baseline, a significant increase in the ADC value was observed in the splenium of the corpus callosum at 11 and 22 hours (20.3 x 10^{-4} mm^2/s to 22.1 x 10^{-4} mm^2/s and 21.9 x 10^{-4} mm^2/s, respectively; $p<0.01$). Similarly, there was a significant rise in the ADC value from baseline in the genu of the corpus callosum at 22 hours (16.9 x 10^{-4} mm^2/s to 18.5 x 10^{-4} mm^2/s, respectively; $p<0.05$). The increase in ADC values within the corpus callosum was noted to occur in all subjects. No significant changes in ADC values were observed in the cerebral or cerebellar white matter. No significant association between a rise in ADC value in the corpus callosum or AMS was observed.

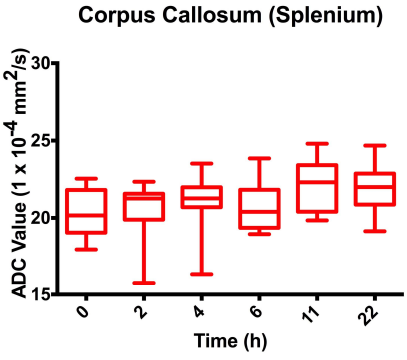

***Fig 2:** Box plot (2.5-97.5 percentile) displaying the trends in ADC values in the splenium of the corpus callosum*

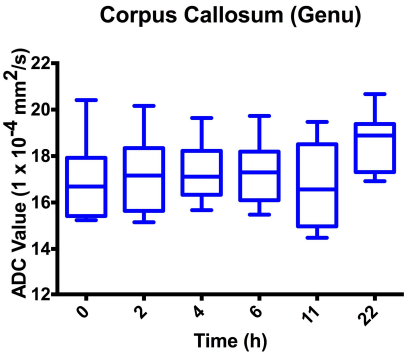

***Fig 3:** Box plot (2.5-97.5 percentile) displaying the trends in ADC values in the genu of the corpus callosum*

Conclusions

As an increase in ADC value represents the development of vasogenic oedema, this study suggests that exposure to normobaric hypoxia results in vasogenic oedema within the corpus callosum. This predilection for the corpus callosum has also been noted in previous studies[2]. However, the rise in ADC value within the corpus callosum was independent of the presence of AMS. No significant changes in ADC values were observed in the rest of the brain. Although a repeat study with a larger number of subjects may be needed to detect significance in varying ADC values elsewhere within the brain, the findings may also suggest that alternative, parallel pathophysiological processes contribute to the symptoms of AMS.

References

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2. Hackett, P, Yarnell P, Hill, R, et al. High-altitude cerebral edema evaluated with magnetic resonance imaging. JAMA.1998;280(22):1920-5