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**Title:** Manipulating cerebral blood flow affects central sleep apnea at high altitude

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**Body:** Background There is an almost universal (>90%) occurrence of central sleep apnea (CSA) in newcomers to high altitude (>5000 m). However, the key factors that determine the severity of CSA upon arrival to high altitude and during acclimatization are not well understood. We hypothesized that cerebral blood flow (CBF) was an important component in the etiology of CSA at high altitude. Aim To measure the effects of altering cerebral blood flow (CBF) on central sleep apnoea (CSA) at high altitude. Methods 12 normal volunteers aged 30 ± 10 years were studied 6-9 days after arrival at 5,050 metres. After control measurements they received i.v. Acetazolamide (Acet) 10mg/kg or oral Indomethacin (Indo) 100mg with placebo controls in a randomized order on separate nights. Ventilatory Responses (VRs), ABGs, Apnea-Hypopnea Index (AHI) during the first 3 hours of sleep by polysomnography (PSG) and CBF by transcranial Doppler were recorded. AHI was also measured upon arrival and after 12-15 days to control for acclimatization. Results CBF rose by 28% with Acet and fell by 23% with Indo. PaCO<sub>2</sub> rose from 28 ± 4 to 31 ± 3 mm Hg with Acet (p<0.001), whereas, ABGs were unchanged with Indo. VRs were unchanged with Acet but Indo increased Hypercapnic VR by 43% (p <0.05). AHI was halved by Acet (89 to 47/hr, (p <0.001), but increased 25% with Indo (89 to 112/hr, p <0.05). Conclusions Indomethacin reduced CBF and increased Hypercapnic VR and CSA during the first 3 hours of sleep. Whereas Acetazolamide increased CBF but had no effect on VRs yet reduced CSA severity. These results highlight the link between CBF and CSA at high altitude. Supported by: Peninsula Sleep Laboratory, University of Otago and EVK2CNR.