Neurovascular coupling is blunted during acute poikilocapnic hypoxia

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Neurovascular coupling (NVC) is responsible for the close temporal and regional linkage of cerebral blood supply to local alterations in cerebral metabolism during neuronal activation and remains an important determinant of cognitive performance. Despite its clinical importance, the mechanisms underpinning hypoxia-induced cognitive impairment remain elusive, but may relate to blunted NVC given the potential of hypoxia to impair cerebrovascular function. To examine this, we measured NVC in twelve healthy participants (11 male and 1 female) aged 28 ± 8 years (mean ± standard deviation) during 30 min of passive exposure to isocapnic normoxia (100 ± 4 mmHg $P_{ET}O_2$ and 43 ± 3 mmHg $P_{ET}CO_2$) and poikilocapnic hypoxia equivalent to a simulated altitude of ~4400m (50 ± 3 mmHg $P_{ET}O_2$ and 27 ± 1 mmHg $P_{ET}CO_2$), achieved through dynamic end-tidal forcing. Posterior cerebral artery blood velocity (PCAv) was assessed using transcranial Doppler ultrasound and beat-by-beat blood pressure for the determination of mean arterial pressure (MAP) via finger photoplethysmography. Following a 60 s supine baseline, all participants completed five consecutive trials of 30 s eyes open with standardised visual stimulation (flashing checkerboard), followed by 30 s of eyes closed. The NVC response was characterised as the percent peak and average increase (relative to the baseline control) in PCAv during 25 s of visual stimulation, averaged across the five trials. Distribution normality was confirmed by Shapiro Wilks W tests and data analysed using paired samples *t*-tests. Poikilocapnic hypoxia reduced baseline PCAv from 42 ± 6 $cm.s^{-1}$ to 33 ± $cm.s^{-1}$ ($P < 0.01$) and attenuated the peak (10 ± 4% *vs.* 16 ± 6%, $P = 0.04$) and average (3 ± 3% *vs.* 7 ± 4%, $P < 0.01$) percent increases in PCAv, across the visual stimulation period. MAP remained unchanged (3 ± 3% *vs.* 3 ± 3%, $P = 0.81$). These are the first data to demonstrate that NVC is blunted following acute poikilocapnic hypoxia in humans. This may potentially be related to hypocapnia-induced vasoconstriction (1) and/or oxidative inactivation of nitric oxide-induced vasodilation (2) that out-competes the normal NVC dilatory mechanisms. A functional attenuation in NVC may contribute to the cognitive deficits observed in patients characterised by arterial hypoxemia and individuals sojourn to terrestrial high altitude.

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