Complex Cognitive Functions and Neurovascular Coupling are Protected by Carbon Dioxide during Hypoxia

Reductions in environmental oxygen availability can impair the performance of cognitively demanding tasks. The compensatory increase in ventilation during hypoxia can have a counterproductive effect on the brain, as reduced arterial carbon dioxide (CO_2) leads to cerebral vasoconstriction and a consequent decline in cerebral oxygen delivery. Providing supplemental CO_2 exerts a protective effect on basic cognitive functions. However, the effects on complex real-world tasks with a greater cognitive demand have yet to be examined. We tested the hypotheses that complex task performance and neurovascular coupling (NVC) would be impaired by poikilocapnic hypoxia, but comparatively protected during isocapnic and hypercapnic hypoxia. Accordingly, twenty-one participants completed a 10-minute simulated driving task whilst breathing room air (normoxia) or hypoxic air ($P_{ET}O_2$ = 45 mmHg) under poikilocapnic, isocapnic, and hypercapnic conditions ($P_{ET}CO_2$ = not manipulated, clamped at baseline, and clamped at baseline +10 mmHg, respectively). Simulated driving performance, assessed using a fixed-base motor vehicle simulator, provided a complex cognitive task. Cortical oxygenation in the frontal cortex was measured using functional near-infrared spectroscopy (fNIRS). The number of road speed limit exceedances was greater during the poikilocapnic than normoxic, hypercapnic, and isocapnic conditions (mean exceedances = 8, 4, 5, and 7, respectively, all $p \leq 0.05$). Mean vehicle speed was greater in the poikilocapnic than normoxic and hypercapnic conditions (mean difference = 0.35 $km.h^{-1}$ and 0.67 $km.h^{-1}$, respectively). Compared to normoxia, prefrontal oxygenation decreased in all hypoxic conditions. During simulated driving, total haemoglobin in the right frontal cortex decreased to a greater extent in poikilocapnic hypoxia compared to normoxic, isocapnic, and hypercapnic conditions (mean decline = 390 %, 280 %, and 200 %, respectively), suggesting that cerebral

blood volume was attenuated to a greater degree in the poikilocapnic condition (i.e., NVC blunted). Collectively, these findings demonstrate that controlling CO_2 availability during severe hypoxia exerts a protective effect on complex cognitive task performance and NVC.