HYPOXIC CHALLENGE ACTIVATES HUMAN SYMPATHETIC BRAINSTEM AND HYPOTHALAMIC SITES

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BACKGROUND: Peripheral carotid chemoreceptors, which raise sympathetic activation at the brainstem level, may be altered trough atmospheric condition and is further affected by weightlessness-induced neural plasticity. However, human peripheral chemoreflex regulation in the brainstem is poorly understood due to the lack of suitable methodologies. Therefore, we combined measurements of beat-by-beat blood pressure and SpO_2, and high-resolution functional magnetic resonance imaging (fMRI) to elucidate human brainstem circuits engaged through hypoxic peripheral chemoreceptor activation.

METHOD AND MATERIAL: We submitted 12 healthy men (29.7 ±6.6 years; 24.0 ±1.86 kg/m^2) to five hypoxic episodes by breathing 10% oxygen for 180 seconds followed by 90 seconds normoxia during multiband fMRI brain acquisitions. We monitored continuous finger arterial blood pressure using customized hardware, ECG, and SpO_2. Brainstem and hypothalamus fMRI images were analyzed to identify nuclei involved in peripheral chemoreflex processing. Systolic blood pressure (SBP) and SpO_2 time courses were correlated with the blood-oxygen-level-dependent signals with a general linear model.

RESULTS: With hypoxia, SpO_2 decreased by 12.32 ±3.68% ($p < 0.01$), heart rate increased 13.86 ±3.47 ($p < 0.01$), and SBP decreased with hypoxia 5.45 ±5.5 mmHg ($p < 0.01$). In the brainstem, the nucleus tractus solitarii (t-values: SpO_2: 5.9; SBP: 4.79), the caudal ventrolateral medulla (SBP: 5.59), intermediate reticular nucleus (SBP: 5.98), nucleus ambiguus (SBP: 5.59), dorsal motor nucleus of the vagal nerve (SBP: 4.79), and inferior olive (SpO_2: 4.7, SBP: 6.16) were identified with high sensitivity and corrected for multiple comparisons ($p < 0.01$). Furthermore, we observed activation of the following hypothalamic nuclei: paraventricular nucleus (SpO_2: 7.67), anterior and lateral hypothalamic area (SpO_2: 7.67, SBP: 4.79), supraoptic nucleus, and tuberomammillary nucleus (SpO_2: 7.07).

CONCLUSION: High-resolution brainstem fMRI during repeated hypoxia traces brainstem circuits engaged by peripheral chemoreceptors. This methodology allows the analysis of neural adaptation to atmospheric conditioning and short- and long term weightlessness. Furthermore, the understanding of the peripheral chemoreceptor contributions to human cardiovascular disease may enlighten not only antihypertensive therapy.