Activation of rat carotid body neurogenic niche by chronic intermittent hypoxia

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Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common disease in the general population. OSAHS patients suffer chronic intermittent hypoxia (CIH) and sympathetic hyperactivity, with increased cardiovascular risk and several comorbidities, including hypertension and insulin resistance, among others. Overactivation of the carotid body (CB), the main arterial O_2-sensing chemoreceptor, by repeated episodes of hypoxaemia is believed to contribute to the pathogenesis of sympathetic hyperactivity present in these patients. The aim of the current study was to investigate whether CIH activates CB neurogenic niche and contributes to the pathogenesis of CB overactivation. An animal model of CIH was applied in which adult male rats were treated with repeated episodes of hypoxia (10% ambient O_2) for 8 hours each day during 14 days. We confirmed sympathetic overactivation in this CIH model by evaluating systemic functional parameters. Using flow cytometry and immunohistochemistry, we have observed a CIH-induced neurogenesis in the CB with activation of neuroblasts, which enter a process of proliferation and differentiation into mature O_2-sensing chemoreceptor glomus cells. Isolation of individual cell classes using cell sorter has allowed us to demonstrate that maturation of CB neuroblasts is paralleled by an upregulation of genes involved in acute O_2-sensing. CIH also enhanced mitochondrial responsiveness to hypoxia in maturing neuroblasts as well as in glomus cells. These data provide novel perspectives on the pathogenesis of CB-mediated sympathetic hyperactivation that may lead to the development of new pharmacological strategies to prevent cardiovascular and metabolic disfunctions in patients with OSAHS.