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CHRONIC INTERMITTENT HYPOXIA INDUCES DEPRESSIVE-LIKE BEHAVIOR IN RATS

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Obstructive sleep apnea (OSA) causes recurrent oxygen desaturation (chronic intermittent hypoxia, CIH) and is associated with depression in patients. However, the relationship between OSA and depression is unclear. Synaptic degeneration, microtubule instability and monoamine deficiency are the common pathological features exhibited in both patients and depression animal models. We hypothesized that CIH induces depressive-like behavior by triggering synaptic degeneration, microtubule instability, and reducing monoamine downstream signaling deficits in the hippocampus. Adult male SD rats were exposed to air (normoxic) control or CIH treatment (8 hours/day) for 7 days. Hippocampus was harvested for the measurement of markers for synaptic vesicle protein (Synapsin I), microtubule stabilizing protein (MAP-2), and monoamine downstream signaling (protein kinase C (PKC), PKC substrate) using Western blot and immunohistochemical staining. Depressive-like behavior was assessed by forced swimming test and sucrose preference test. Immobility time was significantly elevated in the CIH-treated group when comparing to the normoxic control. In addition, sucrose solution consumption was remarkably reduced in the hypoxic group. Protein expression levels of synapsin I and synaptophysin were much less in CIH-treated group than the control. However, MAP-2 protein level was not significantly different between hypoxic and normoxic groups. Furthermore, the number of PKC and PKC substrate positive-labeled cells were significantly reduced by the CIH treatment. In conclusion, CIH induces depressive-like behavior mediated by synaptic degeneration and reduced monoamine downstream signaling.