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EXPLORING MICRORNA-206-3P AS A BIOMARKER IN SPACEFLIGHT-INDUCED DEPRESSION: A NEUROBIOLOGICAL PERSPECTIVE

Abstract

Depression among astronauts poses a substantial challenge stemming from the physiological effects of spaceflight, leading to impairments in cognitive function and work performance. Despite its prevalence, the precise molecular mechanisms underlying spaceflight-induced depression remain incompletely understood. Recently, microRNA-206-3p (miR-206-3p) has been reported to regulate neurological functions in various neuropsychiatric disorders, including depression. However, the interplay of miR-206-3p in space-induced depression remains unexplored. This study aims to elucidate the involvement of miR-206-3p and their interaction with differentially expressed genes (DEGs) in the neurobiological pathways associated with spaceflight-induced depressive behavior. Employing a simulated complex space environment (SCSE) model for a duration of 21 days, depressive behaviour was induced in rats, and the expressions of miRNAs and DEGs in the cortex region of SCSE-exposed rats were assessed using quantitative real-time polymerase chain reaction (qRT-PCR) and high-performance liquid chromatography (HPLC), respectively. Our findings revealed that following 21 days of SCSE exposure, rats exhibited depressive behaviours, including anhedonia (*$p<0.05$), increased immobility (*$p<0.05$), upward climbing (*$p<0.05$), and defecation (*$p<0.05$) compared to the control group. Additionally, analysis of oxidative stress levels indicated an elevation in hydrogen peroxide levels (*$p<0.05$) and a reduction in superoxide dismutase levels (*$p<0.05$) in the SCSE group, suggesting aberrant reactive oxygen species levels in the cerebral cortex. Further investigation demonstrated significant upregulation of miR-206-3p between the SCSE and control groups. Among the 288 differentially abundant proteins identified in the cortex proteome of the SCSE group, 20 DEGs were identified as downregulated targets of the dysregulated miR-206-3p. In-silico analysis of these DEGs unveiled their involvement in critical pathways such as glutamatergic synapse, calcium signaling, and Huntington's disease pathways, implicating their role in the neurobiological mechanisms underlying spaceflight-induced depression. Furthermore, protein-protein interaction analysis identified NMDA receptors such as NR2B, NR2A, NR2B-a, and PSD-95 as the hub genes, influenced by the upregulated

miR-206-3p in SCSE group, pointing to a significant impact of miR-206-3p regulating neuronal functions in SCSE group. In summary, this study provides valuable insights into the potential utility of miR-206-3p as biomarkers for the early diagnosis of mood disorders and neurological abnormalities, thereby advancing health sciences and space healthcare.