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INTERPLAY OF MIRNAS AND DIFFERENTIALLY EXPRESSED GENES IN THE PSYCHOPATHOLOGY OF DEPRESSION UNDER SIMULATED COMPLEX SPACE ENVIRONMENT

Abstract

Depression in astronauts is one of the repercussions of the spaceflight effects, which negatively influence their work performances and cognitive abilities. Unfortunately, the underlying molecular mechanisms in space flight induced depression is still unclear. However, recent studies reported that epigenetic factors especially miRNAs have been involved in various neuropsychiatric disorders, especially depression. However, the role of miRNAs in space induced depression is still not investigated. Therefore, the present study is aimed to investigate the novel insight of candidate miRNAs (miR-455-3p, miR-206-3p, miR-132-3p, miR-16-5p, miR-124-3p and miR-145-3p) with differentially expressed genes (DEGs) in the neurobiology of space induced depressive behavior. Using simulated space environmental model (SCSE) for 21 days, we induced depressive behavior in rats to analyze candidate miRNAs expressions and DEGs in the cortex region of SCSE depressed rats through qRT-PCR and HPLC, respectively. Our results showed that after 21 days of SCSE exposure, the SCSE group showed depressive behavior, exhibiting anhedonia (*p¡0.05), increased immobility (*p¡0.05), and increased upward climbing (*p¡0.05) and defecation (*p¡0.05) than control group. Further analysis of the oxidative stress level showed increased hydrogen peroxide level (*p¡0.05) and lower levels of superoxide dismutase (*p¡0.05), while non-significant changes in malondialdehyde, indicating increased oxidative stress levels in the SCSE group is due to the abnormal ROS levels in the cerebral cortex. Further investigation on miRNAs showed the significantly upregulated expression of miR-455-3p, miR-206-3p, miR-132-3p, and miR-16-5p, with no significant difference in the miR-124-3p and 145-3p expression in SCSE than the control group. The 44 DEGs targets of these dysregulated miRNAs were found downregulated out of 288 differentially abundant proteins in the cortex proteome of the SCSE group. Additional in-silico analysis of these 44 DEGs showed that these miRNAs target genes involved in the glutamatergic signaling pathway, GABA synaptic pathway, long-term potentiation, cAMP signaling pathway, cGMP-PKG signaling pathway and calcium signaling pathway etc., hinting that these miRNAs target are involved in the neuropsychiatry of space induced-depression. Moreover, protein-protein interaction of these DEGs showed PSD-95 as the hub gene, impacting neuronal functions. Overall, this study provided an avenue for the future use of miRNAs as potential biomarkers for the early diagnosis of mood disabilities and neurological abnormalities, thereby providing a great insight for future health sciences and space health care.