

MODERATE TREADMILL EXERCISE PROMOTES NEUROGENESIS THROUGH ENDOGENOUS PACAP/PAC1R SIGNALING IN THE RAT DENTATE GYRUS AND CEREBELLAR CORTEX

N. Palmeri[1], A.G. D'Amico[2], G. Musumeci[1], V. D'Agata[1], G. Maugeri[1]

[1]Department of Biomedical and Biotechnological Sciences, Section of Anatomy, Histology and Movement Science, School of Medicine, University of Catania, Italy; [2]Department of Drug Sciences, University of Catania, Italy

Physical activity (PA) is a recognized non-pharmacological strategy capable of enhancing brain plasticity and stimulating adult neurogenesis. Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP) is a pleiotropic neuropeptide that exerts potent neurotrophic and neuroprotective effects through its high-affinity receptor PAC1R, participating in neural progenitor survival, differentiation, and tissue repair. While exogenous PACAP administration has known limitations due to rapid enzymatic degradation and low blood-brain barrier permeability, lifestyle interventions such as moderate PA may represent an effective physiological approach to stimulate endogenous PACAP pathways. In this study, we investigated whether a moderate treadmill running protocol modulates endogenous PACAP and PAC1R expression, and whether this modulation correlates with markers of neurogenesis in the dentate gyrus (DG) and cerebellar cortex of adult rats. Adult male Wistar rats were divided into sedentary controls and a group subjected to a 12-week moderate treadmill training protocol. Expression levels and topographic distribution of PACAP, PAC1R, and doublecortin (DCX), a marker of immature neurons, were assessed in the hippocampus and cerebellum through immunohistochemistry and Western blot analyses. Confocal immunofluorescence was performed to evaluate PACAP and DCX cellular co-localization. The results demonstrated that moderate physical exercise physiologically upregulates the endogenous PACAP/PAC1R axis and stimulates neurogenic activity not only in the classic hippocampal niche but also in the adult cerebellar cortex. The strict co-localization of PACAP with DCX suggests a functional role for this neuropeptide in exercise-induced neuronal differentiation and structural remodeling, highlighting endogenous PACAP signaling as a key mediator in exercise-driven neuroplasticity.