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THE SYNERGY OF DOPAMINERGIC SYSTEM AND ADULT HIPPOCAMPAL NEUROGENESIS IN A PRE-CLINICAL MODEL OF PARKINSON'S DISEASE

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Depressive disturbances are prevalent in 40% to 50% of clinical cases of Parkinson's Disease (PD), alongside a common reduction in adult hippocampal neurogenesis observed in both PD and its related conditions. This neurogenesis deficit may affect the clinical course of the disease. With this in mind, we set an experiment using the glial fibrillary acidic protein-thymidine kinase (GFAP-TK) transgenic rat model to assess the impact of impaired adult cytogenesis induced by the antiviral Ganciclovir on PD. The experiment involved a combination of the GFAP-TK model and a 6-hydroxydopamine (6-OHDA) model of PD, while behavioral analyses focused on anxiety, depression, and motor skills. From the results, histological examinations revealed decreased proliferative cells and reduced dopaminergic innervation. Additionally, analysis of newborn and immature neurons occurred in the hippocampus, subventricular zone, and olfactory bulbs, while dopaminergic loss was assessed in regions like the substantia nigra and striatum. Findings indicated that the model exhibited anxiety/depressive-like behaviors and motor impairments, linked to the notable loss of dopaminergic neurons, which appeared to correlate with reduced doublecortin-positive cells in the hippocampus. Moreover, results suggested subtle differences between ipsilateral and contralateral sides, highlighting the dopaminergic system's role in hippocampal adaptation. Therefore, these findings suggest a connection between reduced neurogenesis and dopaminergic neuron loss, hinting that these phenomena might be interrelated. Therefore, investigating this potential regional interconnection may augment our understanding of non-motor dimensions in PD pathophysiology related to motor functions, thereby facilitating the development of enhanced therapeutic strategies for individuals in the early stages of PD.

Keyword 1: Depression
Keyword 2: Parkinson's Disease
Keyword 3: Neurogenesis
Keyword 4: Hippocampus