

Pe-006-3 Parkinson's disease model mouse with dorsal striatum lesion with 6-OHDA exhibits cognitive apathy

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Objective: Apathy, a psychiatric symptom of Parkinson's disease (PD), can manifest in several subtypes. However, the pathophysiology and brain regions involved in these subtypes are not well understood. This study investigates the subtypes of apathy and behavioral symptoms in 6-hydroxydopamine (6-OHDA)-lesioned PD model mice, exploring their correlation with pathological changes. Methods: Male C57/BL6J mice were assigned to sham (n=8) and 6-OHDA (n=13) groups. Mice received bilateral dorsal striatum injections of saline or 4 µg 6-OHDA, followed by motor and apathy-related behavioral tests. Tyrosine hydroxylase immunostaining was performed, and correlations between pathological findings and behavioral results were analyzed. Results: The 6-OHDA group exhibited a significant decline in motor function ($p<0.05$). In apathy-related tests, significant differences were observed between the sham and 6-OHDA groups in the hole-board test (HBT) ($p<0.05$) and the novelty-suppressed feeding test ($p<0.05$). The 6-OHDA group showed reduced preference for an inanimate novel object in the three-chamber test ($p<0.05$). Dopaminergic neuron counts in the caudate putamen and substantia nigra compacta (SNc) were significantly reduced in the 6-OHDA group ($p < 0.001$). The head-dip counts in the HBT and SNc neuron counts were positively correlated ($p<0.05$). Conclusion: The PD mouse model exhibited significant dopaminergic neuronal loss and impaired novelty-seeking behavior, a key symptom of cognitive apathy. The levels of dopaminergic neuronal loss may correlate with symptoms of cognitive apathy.