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APPLICATION OF RECOMBINANT VIRAL VECTORS TO PRIMATE BRAIN RESEARCH: GENE THERAPY FOR PARKINSON'S DISEASE

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Using a recombinant adeno-associated virus (AAV) vector, we developed a primate model for Parkinson's disease that was induced by alpha-synuclein (alpha-syn) overexpression in dopaminergic neurons in the substantia nigra pars compacta. Stereotaxic injections of the AAV vector expressing alpha-syn were made unilaterally into the substantia nigra of macaque monkeys. In these monkeys, a battery of motor impairments, such as rigidity, hypokinesia, and tremor, was observed in the limbs on the side contralateral to alpha-syn treatment. Histological analysis exhibited prominent loss of dopaminergic neurons from the substantia nigra. Then, co-injections of the AAV vectors expressing alpha-syn and parkin, the gene causing autosomal recessive juvenile Parkinson's disease, were made into the substantia nigra to examine a protective effect of parkin on parkinsonian insults induced by alpha-syn overexpression. Indeed, parkin recruitment by gene delivery into nigral dopaminergic neurons suppressed motor signs in monkeys treated with alpha-syn. The present results define that parkin can be considered a potential candidate for gene therapy for Parkinson's disease through protection of nigral dopaminergic neurons against degeneration.

Keywords: viral vector, gene delivery, animal model, Parkinson's disease