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PET imaging of gene expression in primate model of Parkinson's disease

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Abstract

Since neurodegenerative diseases such as Parkinson's disease (PD) affect focal regions of the brain, transfer of therapeutic genes to the disease-related regions of the brain has more beneficial than current treatments with systemic administration of drugs. In the present study, we tried positron emission tomography (PET) imaging of local gene expression of aromatic-L-amino-acid decarboxylase (AADC) transferred via adeno-associated viral (AAV) vector into the striatum of MPTP-treated monkeys.

To make bilateral striatal lesions in the brains of Cynomolgus monkeys (*Macaca fascicularis*), MPTP was injected intravenously once a week until a stable parkinsonian syndrome was achieved. PET measurements were performed using a high-resolution animal PET (HAMAMATSU SHR-7700) with [β-^{11}C]L-DOPA, [^{11}C] β-CFT and [^{11}C]SCH23390 for monitoring dopamine (DA) synthesis, transporter and D_1 receptor, respectively. Hand movements in the fine motor task were analyzed by counting the pixels of digital recording with a video camera. After PET studies, the brains were removed and subjected to immunohistochemical assessment.

PET imaging revealed that MPTP-treated monkeys showed complete reduction of presynaptic markers of DA synthesis and transporter availability, whereas no significant changes in postsynaptic marker was detected, as reported previously in Parkinson patients. Three weeks after AAV-AADC injection into right striatum, significantly increased uptake of [β-^{11}C]L-DOPA in the regions, and lasted more than 6 months. Left hand, not right hand, movements were remarkably improved after low dose of L-DOPA administration. Immunoreactivity of AADC was detected in the unilateral putamen of monkeys. These result demonstrated the capability of noninvasive PET imaging for noninvasive assessment of gene therapy.

Biography

Hideo Tsukada has completed his Ph.D. at the age of 27 years from Shizuoka College of Pharmacy. He is the director of PET Center, Central Research Laboratory, Hamamatsu Photonics K.K., a private company supplying photodetectors to major medical equipment companies all over the world. He has published more than 180 papers in reputed journals, being awarded by the Society for Nuclear Medicine (2009), and Japan Molecular Imaging Award (2010), and serving as the visiting professor of two universities.