Dopaminergic Neurons of Human Embryo Transplanted to the Caudate Nucleus of Parkinsonian Monkey — An Immunoelectron Microscopic Study

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There had been many reports on the clinical investigations of transplanting human embryonic ventral mesencephalon for the treatment of Parkinson's Disease patients. However, it is still unable to understand directly how the transplanted human embryonic cells grow and develop in the human brain and the possibility of establishment of synaptic connections with the host. In our past studies, at microscopic level it was seen that dopaminergic neurons of human embryo transplanted into the caudate nucleus of Parkinson's Disease (PD) model monkey could survive and well developed. The present study was to use tyrosine hydroxylase (TH) immunological electron microscopy to check whether there is an establishment of synaptic connections of the transplanted human embryonic dopaminergic neurons with the host neurons of the PD monkey caudate nucleus. Four adult healthy Ganges monkeys were used for this experiment. Injection of 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP, injection dose was 0.7 mg/kg) into right common carotid artery was used to establish PD model. We took artificially aborted human embryo (gestation 11-12 weeks) ventral region of mesencephalon to prepare cellular suspension fluid, injected into many point in the PD monkeys' head of caudate nucleus. To prevent the rejection of the transplanted cells, the host animals were given cyclosporin A etc. immuno-suppressive drugs. Through about one year observation, there was certain degree of improvement in the pathologic symptoms of the PD monkeys which had received the transplant. After perfusion and fixation, caudate nuclei and substantia nigra were subjected to serial vibratome sectioning at 50μm, and the sections were treated with TH immuno-histological reaction. Under microscope it was observed that there was marked reduction of TH positive cells in the right substantia nigra, indicating that the majority of dopaminergic neurons were destroyed. In the right caudate nucleus, TH positive cells of the transplant distributed evenly all over the whole caudate nucleus. Series of bouton like structures with interval of 12 to 20μm were distributed along the whole length of the processes. Furthermore, under dissection microscope, we carefully cut and took the region with strong TH reactivity, embedded for electron-microscopy and ultrathin sections were obtained for transmission electron microscope observation. It could be seen that TH positive cell bodies formed connections with negative dendritic trunks and dendritic spines, positive dendrites formed connections with negative dendrites and axons terminal boutons, TH positive axon terminal boutons formed connections with negative dendritic trunk, dendrite spine and axon terminal boutons also formed synaptic connections. Most of the