Allograft of Stem Cell-Derived Dopaminergic Neurons for Parkinson's Disease


The proposal to replace the lost dopaminergic neurons of patients with Parkinson’s disease (PD) with new ones emerged in the 1970s. This strategy may be anticipated to restore motor functions. However, previous clinical studies using fetal midbrain tissue reported mixed outcomes (for a review, see Bjorklund and Kordower1). Promising results were obtained from embryonic stem (ES) cell-based studies, but a major concern in the use of ES cells is the risk of tumor growth.

The groups led by Yasuhiko Tabata and Mari Dezawa previously reported a method to efficiently differentiate A9 dopaminergic neurons from bone marrow-derived mesenchymal stem cells (MSCs), a type of adult stem cell, offering potential for autologous cell therapy. In the study by Hayashi and colleagues, the authors engrafted dopaminergic neurons derived from MSCs in hemiparkinsonian macaque monkeys. Animals derived a very modest motor improvement, which was only significant at 8 months after surgery. Positron emission tomography with a dopamine transporter ligand produced an important increase 7 days after surgery followed by an exponential decrease over time. The authors determine a 0.3-month half-life of the grafts, explaining the minor improvements in motor function. Tumorigenicity also was assessed by positron emission tomography and blood analysis, and no tumor formation was identified, as later confirmed ex vivo. Postmortem analysis of the brain tissue revealed that engrafted neurons maintained an A9 dopaminergic neuron phenotype for 9 months.

Despite the small improvement in motor function of the engrafted parkinsonian monkeys and the need for further developments to increase graft viability, the reported system might expand the availability of material without strong ethical concerns for cell-based therapy. Putting these results in context with recent reports that human fibroblasts can be converted directly to dopaminergic neurons, avoiding the pluripotent cell step, it is possible that allografting may represent a safe and effective cell-based strategy for the treatment of PD.

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