Editorial
Volume 12:6, 2021

Journal of Tissue Science and Engineering

ISSN: 2157-7552 Open Access

A Note on Functional Neuronal Transplantation

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Editorial Note

In the last four decades, Functional Neural Transplantation has come a long way. During the 1970s and early 1980s, pioneering studies established basic methods for achieving effective survival and integration of embryonic neuronal tissue grafts in the mammalian central nervous system, resulting in the publication of three major review volumes covering this new field in quick succession in the early 1980s. Their main focus was on establishing the technical components of delivery, demonstrating neuronal survival, describing the anatomical growth of connections between transplanted cells and the host brain, and developing the first biochemical, physiological, and basic assessments of function. From the start, researchers wanted to see if functional recovery in basic animal models may pave the path for novel surgical procedures to treat hitherto untreatable neurological diseases in humans.

The ability of neural transplants to alleviate functional deficits in animal models of a variety of neurodegenerative diseases had been well established by the early 1990s, and the feasibility of translation had been dramatically established by the first demonstration of unequivocal functional benefit in Parkinson's disease, at least for some patients. This led us to co-edit the first major review volume, Functional Neural Transplantation, which focused explicitly on the range of animal models that were then being used to evaluate the functional efficacy of neural grafts, exploring the mechanisms and conditions for functional recovery, and summarising the first clinical applications, most notably in Parkinson's disease, but also looking forward to applications in a range of other conditions, such as Huntington's disease.

Although the first human embryonic stem cell lines were clearly on the horizon, they had not yet translated to functional transplantation even in animal models; alternative sources of cells were now being examined, including immortalised cell lines, cell encapsulation, and xenotransplantation. Clinical trials had already begun in a number of different disorders, including Huntington's disease, retinal disease, ischemia, and spinal cord damage, with mixed results, but the focus remained on primary foetal cells.

The past decade has seen major swings in the fortunes of functional cell trans-plantation, in both negative and positive directions. On the one hand, the first double-blind placebo-controlled research of cell transplantation found very limited indications of efficacy, as well as the onset of substantial adverse effects in the form of graft-induced dyskinesias in some of the grafted patients. Despite the fact that this has cast a significant cautionary cloud over the field of using primary foetal neural tissues for cell therapy, particularly in the treatment of Parkinson's disease, more substantive trials in Huntington's disease, stroke, pain control, spinal cord injury, ALS, and macular disease have emerged.

On the other hand, significant progress has been made in understanding normal neuronal differentiation in the developing embryo, allowing for the directed differentiation of stem cells toward a variety of specific neuronal fates, which is required to provide alternative neuronal populations for transplantation. Adult somatic stem cells, the creation of induced pluripotent stem cells, and even direct transdifferentiation of neuronal cells from differentiated cells of various non-neuronal lineages have all been found as sources of pluripotent cells.

Stem cells now have a realistic chance of becoming a viable alternative source of cells for cell replacement therapy, avoiding the difficult ethical, logistical, immunological, and quality control difficulties that come with using primary fetal tissues.

How to cite this article: Nicholas, Robinson. "A Note on Functional Neuronal Transplantation ." *J Tiss Sci Eng* 12 (2022) : e009.

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Received: December 15, 2021; **Accepted**: December 29, 2021; **Published**: January 05, 2022