Introduction to Suspension Grafting Procedure

Robinson Nicholas*

Department of Biomedical Engineering, University of Memphis, Tennessee, United States

About the Study

With the introduction of the suspension grafting process, it is now possible to reliably transplant neurons into any part of the adult brain. This has opened up hitherto inaccessible areas of the brain for transplantation and enabled a variety of new possibilities. One such outcome is the ability to replace the constituent neurons of a brain nucleus *in vivo*. Another advantage of this grafting procedure, as we've seen with dopaminergic innervation of the caudate-putamen, is that clusters of grafted neurons can now be placed directly into target locations where innervation would be most effective. Moreover, by distributing multiple deposits of neurons throughout a target area, very large brain regions can be re-innervated, and with a greater density than possible with other grafting procedures.

This in turn, as demonstrated by sensorimotor testing, results in greater functional compensation. The procedure is designed in such a way that grafting may be done without removing cortical tissue, as cavity implant techniques require, and even numerous grafts can be done with minimal disturbance to the host brain. With the suspension grafting procedure, as well as with other grafting methods, there are many different neuron types included in the grafts. In this reference, with the suspension grafting procedure, it may prove possible to selectively sort the dissociated donor tissue into individually identified neuron types before grafting. One basic method, as demonstrated with cerebellar grafts, is to take advantage of the influence of donor age on neuron survival. This should, in theory, work for any neuron type that is the last to emerge in neural tissue. Future possibilities for neuron selection may include fluorescenceactivated cell sorting, differential centrifugation, the use of mitotic inhibitors, selective re-aggregation or substrate adherence, and an intermediate step with neuron culture. A further extension of this capability would be to investigate the developmental and functional consequences of selective recombination of individual neuron types and/or glia. Despite the apparent superiority of the suspension grafting approach in a variety of reinnervation settings, solid grafting procedures have their own set of advantages in particular circumstances. The ability to find solid grafts within the brain for electrical stimulation and recording, as well as the injection of tracer chemicals to illuminate afferent and efferent connections, has already been demonstrated. Another interesting use of solid grafts has been to make it easier for regenerated axons to cross lesion areas and reach their target fields.

Solid grafts including the locus coeruleus have also been shown to be a successful technique to restore noradrenergic innervation to target brain locations, however, it appears that locus coeruleus cells do not readily survive suspension grafting. The reasons for the disparity are unknown. The recognition processes required for particular nerve development are unaffected by dissociation.

This shows that, at least for the neuron types studied thus far. specificity information is internal to individual cells and not dependent on the three-dimensional arrays that are commonly encountered. These neuron transplant findings are backed up by discoveries of proper growth specificity in nigral neurons cultivated with various target and non-target tissues. The specificity of reinnervation, however, is not total. Lesions that denervate an unrelated afferent pathway in the target can cause inappropriate as well as accelerated development from neuron transplants. Outgrowth from neuron grafts may thus respond in part, according to a hierarchy of specificities, to the availability of vacant synaptic space in the target. Neurotrophic factors, which stimulate nerve development with variable relative specificities, may be produced as a result of denervating lesions. Further research using neuron grafts should substantially aid in the identifying of factors that determine the growth of neuronal processes. Many basic elements of neuron growth and brain development are already being studied and understood using these techniques. The expanding number of studies that show appropriate functional activity innervated systems, even at the behavioral level, clearly indicates that clinical applications in the treatment of some neurodegenerative illnesses may be possible in the future. While suspension grafting is the most effective method for re-innervation in many target areas, further refinement of the procedure will necessitate detailed quantitative studies on cell survival and proliferation, as well as the development of methods to obtain relatively purified preparations of the desired donor neurons. Another set of concerns involves determining the immunological limitations of neuron transplantation, locating suitable sources of donor tissue, and preserving such tissues in an active state until they are needed. One intriguing strategy is to investigate the use of autologously generated tissues such peripheral ganglia or adrenal medullary cells. Finally, it is important to note that transplanting neurons into ectopic sites in the brain or elsewhere may have

*Address for Correspondence: Dr. Robinson Nicholas, Department of Biomedical Engineering, University of Memphis, Tennessee, United States; E-mail: robin22@nicolas.edu

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substantial functional or behavioral consequences. The current availability of easy and dependable techniques for grafting live neural tissue into the brain is a major accomplishment.

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