EARLY AND LATE POST-MORTEM NEURAL STEM CELLS GROW AND DIFFERENTIATE IN VITRO. A NOVEL SOURCE FOR CELLULAR TERAPHY

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Spinal cord injury (SCI) often results in significant neurological dysfunction and disability. An annual incidence of 15 to 40 traumatic SCI cases per million has been reported worldwide.
Since the isolation of neural stem cells (NSCs) from various regions of the mammals brain, several new sources of NSCs for cellular therapy of various neural degenerative conditions have been studied. Here we report that a possible supply is represented by post mortem explants of brain tissue. With this purpose we have defined appropriate methods for the isolation, expansion and characterization of neural stem cells from mice several hours after death (PM-NSCs).
The isolation was performed from 2 up to 16 hours from the death of the donor animal. We characterized these cells for their proliferation and differentiation capabilities. Following transplantation in a mouse model of spinal cord injury by intravenous administration, we observed a significant promotion of recovery of function..
The PM-NSCs, obtained at 2, 4, 6, 16 hours after death of the donor mice, have a comparable growth and proliferation ability, that is comparable to that of control NSC (cNSC) (obtained from tissue that was promptly isolated after the mice euthanasia). Interestingly, however, the process of differentiation resulted different since the percentage of neurons in PM-NSCs is markedly higher than with cNSC. The i.v. administration of 1.000.000 Post Mortem-NSCs prepared 6 hours after mouse death significantly improved the rate of recovery of hind limb function (evaluated by the Basso Rating Scale (1)) when compared with animals treated with saline solution. Maximum extent was achieved within 4 weeks and maintained up to 180 days.
In conclusion NSCs survive in the SVZ of the mouse up to 16 hours after death, and when isolated have growth characteristics similar to those of cNSC; on the other hand following in vitro differentiation there is a much higher yield of neurons. When applied to spinal cord injured mice, there is a great enhancement in the rate of recovery. Thus we suggest that PM-NSCs may represent a good source for cellular therapy in neurodegenerative disorders.

Bibliografy

1. Basso, D. M., Fisher, L. C., Anderson, A. J., Jakeman, L. B., McTigue, D. M. & Popovich, P. G. (2006) J Neurotrauma **23,** 635-59.