Mitochondrial Transplantation Following Contusion Spinal Cord Injury

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The current study tested whether transplantation of exogenous mitochondria into the contused rat spinal cord results in 1) their incorporation into various host cell types, 2) improving overall bioenergetics of host cells, and 3) increasing long-term functional neuroprotection. For visualization of transplanted mitochondria, we used transgenically modified PC12 cells in which mitochondria were labeled with tGFP, and for clinical relevance, we also used mitochondria isolated from rat soleus muscle. Freshly isolated tGFP (50, 100 or 150 µg/cord) or muscle (50 or 100 µg/cord) mitochondria were microinjected into the penumbra of severely contused spinal cords within 1 hr after spinal cord injury (SCI) at L1/L2 (250 kdyn using IH Impactor) in adult female Sprague-Dawley rats. Depending on outcome measures, they survived 24 hr, 48 hr, 7 days or up to 6 weeks. Results showed that transplantation of either tGFP or muscle mitochondria significantly maintained bioenergetics of injured spinal cord tissues 24 hr after injury, with maximum effects at the 100ug dosage. Confocal imaging showed prominent rostro-caudal spread of exogenous tGFP mitochondria from injection sites after 24-48 hr that dissipated by 7 days. At the earlier time points, tGFP mitochondria co-localized conspicuously with microglia/macrophages and endothelial cells, with less incidences in astrocytes and oligodendrocytes, and none in neurons. Assessments of hindlimb functional recovery (BBB-LRS) and paw withdrawal latencies (Von Frey hair) over 6 weeks after transplanting 100ug tGFP or muscle mitochondria showed no significant differences in over-ground locomotion or mechanical hypersensitivity compared to vehicle-injected injured groups. Morphometric analyses further showed no differences in grey or white matter tissue sparing. In summary, intraspinal injections of mitochondria after contusion SCI improved cellular bioenergetics acutely, but such maintenance of respiration did not translate into improved long-term functional neuroprotection.

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