NEURORESTORATIVE TREATMENTS OF EXPERIMENTAL CNS INJURY

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Treatment of both central nervous system and peripheral nervous system neurological injury and neurodegenerative diseases have historically focused on protection, reducing the extent and intensity of injury and disease. A plethora of neuroprotective agents, primarily for injury/disease of the CNS, such as stroke, traumatic brain injury (TBI) and multiple sclerosis (MS), have met with clinical failure. A different approach, primarily, not to treat injury, but to enhance endogenous restorative effects, often accompanying injury/disease may be more fruitful, and lead to what is of primary interest, improvement and possibly restoration of neurological outcomes, post neural-injury/disease. Here, I will review some of our research on the use of cell-based and pharmacological neurorestorative and delve into molecular mechanisms underlying their therapeutic efficacy. Preclinical data on stroke, TBI, MS, diabetic brain post stroke, and diabetic peripheral neuropathy will be presented, demonstrating that restorative agents may be highly efficacious in the remodeling of the central and peripheral nervous systems, promoting neurovascular remodeling, and thereby neurological recovery over a broad range of neurological disease/injury. Stem cell-based therapies have been widely investigated as a means to enhance neurological recovery I will demonstrate that stem-like cells encapsulate miRNAs within tiny lipid particles, exosomes (~40-100nm). microRNAs, are master molecular switches-that regulate gene translation and subsequently many biological processes. Thus, exosome cargo containing miRNAs transfer key genetic regulatory instructions to tissue adjacent to and remote from the stem cells. The exosome/miRNA communication network underlies a vast arena of biological processes and may be employed to promote recovery post neural injury. The bases of cell-based and restorative therapeutic efficacy may reside in their modulation of exosomes/ microRNAs subsequently evoke multifaceted restorative impact.