NEURAL STEM CELLS AS A THERAPEUTIC FOR KRABBÉ’S DISEASE.


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Krabbe’s disease is a degenerative neurological disorder with rapidly progressive demyelination of the central and peripheral nervous system. It is a lysosomal storage disease that results from an autosomal recessive mutation in the galactocerebrosidase (GALC) gene which severely affects the activity of the enzyme. To date there is no cure for Krabbe’s disease, though hematopoietic cell transplantation prolongs lifespan, delays the onset of symptoms and also decreases the severity of the disease in human patients. However, the hematopoietic cell treatment must be administered before the development of any symptoms and this is often complicated by graft versus host disease.

Neural stem cells (NSCs) are self-renewing multipotent cells that generate the main phenotypes of the nervous system. Recent progress in NSC research has shed light on the possibility of repair and restoration of neuronal function in neurodegenerative diseases using these cells. Mouse NSCs from the subventricular zone of eGFP transgenic mice were transplanted into the lateral ventricles of 3-4 days old twitcher mice, the murine model of Krabbe’s disease. The transplanted cells could be traced to various parts of the brain until 16 days post injection. Injecting the mice with NSCs led to an increase in both lifespan and body weight, as well as modest improvements in motor function. After euthanization, the brain and spinal cord were collected and various molecular tests were performed. The NSCs appeared to dampen the inflammation associated with this disease. Results revealed that the level of pro-inflammatory cytokines and chemokines decreased, along with down-regulation of iNOS. There was also less macrophage infiltration and microglial activation. Additionally, the NSCs increased myelin levels and GALC enzyme activity in the brains of the treated mice.

Overall, the NSCs led to promising improvements in the twitcher mice, especially at the molecular level. In spite of this progress the mice still deteriorated and died with symptoms indistinguishable from untreated controls. The evidence suggests that this treatment may only target the central nervous system and that the improvements in the brain may be overshadowed by the deterioration of the peripheral nervous system. A combination therapy approach and systemic administration may be necessary to improve the outcome of NSC treatment.