

Human neural precursor cells promote neurologic recovery in a viral model of multiple sclerosis.

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Public Summary:

This study was based on a surprise result. We transplanted neural precursor cells (NPCs) that we derived from human pluripotent stem cells into the spinal cords of mice that were paralyzed with symptoms similar to severe MS. This was a control rather than an experiment; we expected that the human cells would be rejected, and they were, in a week. What we didn't expect was that the transplanted cells would cause dramatic changes in the mice. Inflammation in the spinal cord disappeared, and the oligodendroglial cells rewrapped the nerve fibers with myelin. The mice recovered almost completely from the paralysis after just 3 weeks, and after 6 months, they ran around their cages as if they'd never been paralyzed. We followed up on this surprise result by analyzing exactly what the transplanted cells were doing during their short time in the mouse spinal cord. We have identified several proteins made by the cells that we think may be responsible for the recovery. We're now testing that idea and hope that this research will eventually lead to a novel treatment for MS.

Scientific Abstract:

Using a viral model of the demyelinating disease multiple sclerosis (MS), we show that intraspinal transplantation of human embryonic stem cell-derived neural precursor cells (hNPCs) results in sustained clinical recovery, although hNPCs were not detectable beyond day 8 posttransplantation. Improved motor skills were associated with a reduction in neuroinflammation, decreased demyelination, and enhanced remyelination. Evidence indicates that the reduced neuroinflammation is correlated with an increased number of CD4(+)CD25(+)FOXP3(+) regulatory T cells (Tregs) within the spinal cords. Coculture of hNPCs with activated T cells resulted in reduced T cell proliferation and increased Treg numbers. The hNPCs acted, in part, through secretion of TGF-beta1 and TGF-beta2. These findings indicate that the transient presence of hNPCs transplanted in an animal model of MS has powerful immunomodulatory effects and mediates recovery. Further investigation of the restorative effects of hNPC transplantation may aid in the development of clinically relevant MS treatments.

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