Study Supports Intracerebral Stem Cell Injections to Prevent/Reduce Post-Stroke Cognitive Deficits

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Innovative strategy reported in Restorative Neurology and Neuroscience

Cognitive deficits following ischemic stroke are common and debilitating, even in the relatively few patients who are treated expeditiously so that clots are removed or dissolved rapidly and cerebral blood flow restored. A new study in Restorative Neurology and Neuroscience demonstrates that intracerebral injection of bone-marrow-derived mesenchymal stem cells (BSCs) reduces cognitive deficits produced by temporary occlusion of cerebral blood vessels in a rat model of stroke, suggesting that BSCs may offer a new approach for reducing post-stroke cognitive dysfunction.

According to the American Heart Association, almost half of ischemic stroke survivors older than 65 years of age experience cognitive deficits, contributing to functional impairments, dependence, and increased mortality. The incidence of cognitive deficits triples after stroke and about one quarter of cognitively impaired stroke patients' progress to dementia. For these reasons, "there is an underlying need for restorative therapies," says lead investigator Gary L. Dunbar, PhD, of the Field Neurosciences Institute Laboratory for Restorative Neurology, and Director of the Central Michigan University Program in Neuroscience.

In order to see whether mesenchymal stem cells derived from bone marrow could attenuate or prevent cognitive problems following a stroke-like ischemic event, the investigators mimicked stroke in rats by injecting the hormone endothelin-1 (ET-1) directly into the brain in order to constrict nearby blood vessels and block blood flow temporarily. Control animals underwent similar surgery but were injected with saline, not ET-1.

Seven days after the "stroke", some of the rats received intrastriatal injections of BSC, while others received control injections. Cognition was evaluated using a spatial operant reversal task (SORT), in which the animals were trained to press a lever a certain number of times when it was illuminated to receive a food reward.

The investigators found that animals that underwent a stroke but were then injected with BSC made significantly fewer incorrect lever presses than stroke rats who received control injections. In fact, the BSC-treated stroke animals performed as well as those who did not have a stroke. "Importantly, there were no significant between-group differences in the total number of lever presses, indicating the deficits observed were cognitive, rather than motor in nature," said Dr. Dunbar. No differences were observed in infarct size between the BMMSC-treated and control groups.

The authors emphasize that the BMMSCs were effective even when transplanted seven days after the induced stroke, a finding that offers hope to patients who may not present for treatment immediately. The authors suggest that BMMSCs may work by creating a microenvironment that provides trophic support to remaining viable cells, perhaps by releasing substances such as brain-derived neurotrophic factor (BDNF).

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