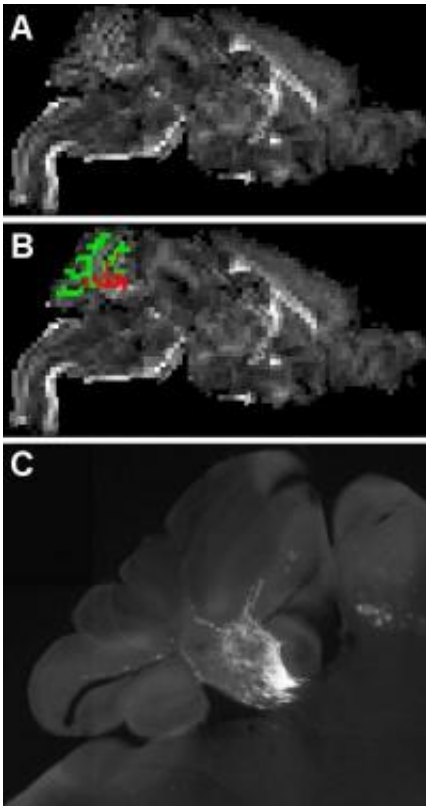


Human neural stem cells study offers new hope for children with fatal brain diseases

October 10 2012



A. This is a high-field MRI scan of the entire brain of a mouse that received the transplant of human stem cells (HuCNS-SCs; spinal cord is at lower left and the front of the brain is far right) B. The red color identifies regions in white matter where the MRI signal predicted that stem cells made new myelin. Green areas predicted no myelin. C. An analysis for human myelin was done in the region of the brain seen on the MRI in red and green in panel B. Regions in white confirmed that myelin was present where predicted by the MRI signal in panel B. Credit: Oregon Health & Science University Doernbecher Children's Hospital

Physician-scientists at Oregon Health & Science University Doernbecher Children's Hospital have demonstrated for the first time that banked human neural stem cells—HuCNS-SCs, a proprietary product of StemCells Inc.—can survive and make functional myelin in mice with severe symptoms of myelin loss. Myelin is the critical fatty insulation, or sheath, surrounding new nerve fibers and is essential for normal brain function.

This is a very important finding in terms of advancing stem cell therapy to patients, the investigators report, because in most cases, patients are not diagnosed with a myelin disease until they begin to show symptoms. The research is published online in the journal *Science Translational Medicine*.

Myelin disorders are a common, extremely disabling, often fatal type of brain disease found in children and adults. They include cerebral palsy in children born prematurely as well as multiple sclerosis, among others.

Using advanced MRI technology, researchers at OHSU Doernbecher Children's Hospital also recently recognized the importance of healthy brain [white matter](#) at all stages of life and showed that a major part of memory decline in aging occurs due to widespread changes in the white matter, which results in damaged myelin and progressive senility (*Annals of Neurology*, September 2011).

In this breakthrough study, Stephen A. Back, M.D., Ph.D., senior author and clinician-scientist in the Papé Family Pediatric Research Institute at OHSU Doernbecher Children's Hospital, used a transgenic mouse model (Shiverer-immunodeficient) that develops progressive neurological deterioration because it is unable to make a key protein required to make normal myelin. Although this mouse has been widely investigated, prior to this study, true human brain-derived [stem cells](#) had not been tested for their potential to make new myelin in animals that were already

deteriorating neurologically.

"Typically, newborn mice have been studied by other investigators because stem cells survive very well in the newborn brain. We, in fact, found that the stem cells preferentially matured into myelin-forming cells as opposed to other types of brain cells in both newborn mice and older mice. The brain-derived stem cells appeared to be picking up on cues in the white matter that instructed the cells to become myelin-forming cells," explained Back.

Although Back, in collaboration with investigators at StemCells Inc., had achieved success implanting stem cells in presymptomatic newborn animals, it was unclear whether the cells would survive after transplant into older animals that were already declining in health. Back and his colleagues put these cells to the test by transplanting them in animals that were declining neurologically and found that the stem cells were able to effectively survive and make functional myelin.

The study also is important because the research team was able to confirm by MRI that new myelin had been made by the stem cells within weeks after the transplant. Until now, it was unclear whether stem cell-derived myelin could be detected without major modifications to the stem cells, such as filling them with special dyes or iron particles that can be detected by the MRI.

These studies were particularly challenging, Back explained, because the mice were too sick to survive in the MRI scanner. Fortunately, OHSU is home to a leading national center for ultra-high field MRI scanners that were used to detect the myelin made by normal, unmodified stem cells.

"This is an important advance because it provides proof of principle that MRI can be used to track the transplants as myelin is being made. We actually confirmed that the MRI signal in the white matter was coming

from human myelin made by the stem cells," Back said.

In a study conducted by clinical researchers at the University of California San Francisco and [published in the same online issue](#) of *Science Translational Medicine* (Gupta et. al), the human neural stem cells were also tested in a small number of patients with a rare childhood myelin disorder where the MRI was detecting signals from the brain consistent with myelin formation. Before MRI, there wasn't a way to confirm new myelin without a brain biopsy or an autopsy. The USCF researchers report the study results strongly support that the MRI findings in the patients were due to new myelin.

"These findings provide us with much greater confidence that going forward, a wide variety of myelin disorders might be candidates for therapy. Of course, each condition varies in terms of severity, how fast it progresses and the degree of brain injury it causes. This must all be taken into consideration as neurologists and stem cell biologist work to make further advances for these challenging [brain](#) disorders," Back said.

Provided by Oregon Health & Science University

Citation: Human neural stem cells study offers new hope for children with fatal brain diseases (2012, October 10) retrieved 7 May 2024 from <https://medicalxpress.com/news/2012-10-human-neural-stem-cells-children.html>

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