Newly developed cell transplantation delivery method could treat traumatic brain injury

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Treating traumatic brain injury (TBI) using stem cell therapy is an important area of current research. However, injecting stem cells into the central nervous system has serious drawbacks, including intracranial hemorrhage and cells failing to reach TBI-affected areas of the brain.

Now, a research team from the University of Maryland, Baltimore and the Veterans Administration Maryland Healthcare System has successfully directed human neural progenitor cells (hNPCs) to injured brain areas by labeling them with iron-oxide "superparamagnetic nanoparticles" and guiding them to the site of injury using a magnetic field. Tested on rats modeled with TBI, they found that the magnetic field delivery method does not affect the viability of hNPCs and that the method provides both increased homing to the injury site as well as retention of the transplanted cells.

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line.

"Magnetic cell targeting is ideally suited to augmenting cell therapies," said study lead author Dr. Paul Yarowsky, of the University of Maryland School of Medicine and the VA Maryland Healthcare System. "The external magnetic field and field gradient can guide cells to sites of injury and, using MRI, the iron-oxide superparamagnetic nanoparticles can be visualized as they travel to the site of injury. The goal when employing this method is not only guiding the particles to the site of injury, but also enhancing entry into the brain and the subsequent

retention of transplanted cells."

The researchers reported that the intensity of the magnetic field does not affect the in vitro viability, proliferation or differentiation of cells loaded with iron oxide nanoparticles. These results, said the researchers, suggest that the method is a "promising technique" for cell delivery in TBI and other neurological injuries and neurodegenerative diseases.

Questions remain, however. For example, what happens to the transplanted stem cells when the magnetic field is no longer present? Also, what are the limits to magnetic intensity - could the cells "clump" together in a more intense magnetic field? Additionally, what is the minimum length of time the "magnetic hat" must be in place for successful cell transplantation?

Although the optimized magnetic intensity obtained for small animal studies must be extrapolated to larger animals, the researchers concluded that "taken together, our results show that magnetic retention of labeled particles is a promising cell therapy for delivery in TBI with potential for clinical translation."

The researchers are currently assessing long-term changes in hNPC viability and differentiation following magnetic retention, and also investigating the transplant method's enhancement of functional recovery following TBI.

"The significance of this study lies in the fact the method used circumvented the need for invasive transplantation procedures, such as intracerebroventricular injection," said Dr. John R. Sladek, Jr., professor of Neurology, Pediatrics, and Neuroscience, Department of Neurology at the University of Colorado School of Medicine and section editor for *Cell Transplantation*. "Furthermore, use of a magnetic field to increase homing of cells, which can be problematic, to the target tissue proved

efficacious. Future studies should explore whether this method would be safe and effective for humans, as it would necessitate a more intense magnetic field in order to increase migration of cells to deeper regions of the brain parenchyma."

More information: Shen, W.-B.; Plachez, C.; Tsymbalyuk, O.; Tsymbalyuk, N.; Xu, S.; Yarnell, D.; Mullins, R.; Gulapalli, R.; Puche, A.; Simard, J. M.; Fishman, P. S.; Yarowsky, P. Cell-based therapy in TBI: Magnetic retention of neural stem cells in vivo.. Cell Transplant. Appeared or available on-line: September 21, 2015. ingentaconnect.com/content/cog … t-CT-1424_Shen_et_al

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