Transplanted brain cells hold promise for Parkinson's disease

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Dr. Cesario V. Borlongan, neuroscientist at the Medical College of Georgia. Credit: Medical College of Georgia

Transplanted neural stem cells hold promise for reducing the destruction of dopaminergic cells that occurs in Parkinson's disease and for replacing cells lost to the disease, scientists say.

Research published in the current issue of *The Journal of Neuroscience* shows a human neural stem cell transplant essentially enables an animal model for Parkinson's to continue functioning normally rather than displaying the progressive loss of movement control that characterizes the disease.

"We are very cautious but to us, it's an indication that stem cells have promise for Parkinson's disease," says Dr. Cesario V. Borlongan, neuroscientist at the Medical College of Georgia and corresponding author of the study.

Transplants were done shortly after a neurotoxin was used to destroy neurons that make dopamine, a neurotransmitter key to movement control, Dr. Borlongan notes. This would be equivalent to a patient getting treatment very early in the disease process, which rarely happens since there is no screening test to catch it early.

"Right now we are saying if you are able to identify Parkinson's in the early stage, we think this therapy will work. An important question that remains is, 'Can we rescue neurons that are dying from Parkinson's'" This would more accurately mimic what patients need." The researchers already have begun studies that delay the transplants until weeks after injury.

For this study, researchers compared animals that received placebo treatment with those that received only protective neurotrophic factors secreted by stem cells and those that had a transplant.

Animals that received transplants essentially regained control of their movement, placebo-treated animals did not recover and those that received neurotrophic factors, called stem cell factors, recovered partially.

When researchers examined the brains one month after transplant – a long time in the two-year life of a rat - researchers found endogenous dopaminergic cells and transplanted neural stem cells had both survived. Also, transplanted neural cells had formed synapses to communicate with each other and ultimately the striatum, the portion of the brain dopaminergic cells act on to control movement.

"When we looked at the transplanted stem cells, they had survived, had differentiated into neurons and showed some connection with the host tissue," says Dr. Borlongan.

They did additional studies in test tubes, taking commercially available rat and human dopaminergic cells, exposing them to neurotoxins and then to stem cell factors. Stem cell factor protected cells in a dose-dependent fashion. "The more stem cell factor, the better the protection," Dr. Borlongan says. When the cells were co-cultured with stem cells, protection was further increased. When they used an antibody to block the stem cell factor, neuro-protection was significantly reduced. "This again shows a combination of factors at work," says Dr. Borlongan. "It's a synergistic effect."

He's now following rats with transplants for six months to see if the early protection/recovery holds up; he's already past the three-month mark and to date, recovery is stable. While the rats needed immunosuppression because they received human cells, Dr. Borlongan says humans would not.

About a half-million Americans have Parkinson's disease. Typically the disease does a lot of damage to dopaminergic cells before it becomes symptomatic. Although Parkinson's is associated with abnormal movement, such as tremors, loss of these cells actually makes it difficult for people to move and, once they move, they can't control the movement, Dr. Borlongan says. The standard treatment is L-dopa, a synthetic dopamine that tends to minimize symptoms for three to five years. As the disease progresses and the drug becomes less effective, doses are increased and can produce more dyskinesia, loss of controlled movement. Centers such as MCG are exploring new ways to slow disease progression, diagnose it earlier and more accurately monitor its progression.

Source: Medical College of Georgia