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Dementia with Lewy bodies may one day be treatable with stem cells

Hopes of a treatment for dementia with Lewy bodies have been raised after a new study showed that stem cells transplanted into mice dramatically improved the motor and cognitive impairments associated with the brain-wasting disease.

The researchers, including neurobiologists from the University of California-Irvine (UCI), published their study in the journal *Stem Cell Reports*. While there is still a long way to go, the researchers hope **stem cell** transplants will one day be used to treat **dementia** with Lewy bodies in human patients.

The term dementia is used to describe the cognitive impairment or loss of mental ability that results from death of brain cells. It rarely strikes before the age of 65.

Dementia with Lewy bodies (DLB) is estimated to account for 10-25% of dementia cases, and is thought to be the most common cause of dementia following **Alzheimer's disease** and vascular dementia.

Like people with Alzheimer's disease, people with DLB experience problems with memory and judgment. But unlike Alzheimer's disease, DLB also causes problems with concentration and visual perception, such as being able to judge where objects are in space.

DLB is caused by deposits of a protein called alpha-synuclein that collects into spherical masses called Lewy bodies in the brain. This also happens in **Parkinson's disease**. The protein deposits cause brain cells to malfunction, alter brain chemicals, and disrupt communication between brain cells, resulting in death of brain cells.

Transplanted stem cells improved motor, cognitive function in mice

Because DLB kills brain cells, the researchers had the idea that it may be possible to use stem cells to regenerate new brain cells in the areas damaged by the disease. So they set out to test the idea in mice.

For their study, the team transplanted mouse brain stem cells into mice genetically engineered to develop many of the key features of DLB.

A month after the transplants, they put the mice through various behavior tests and compared the results with how they performed before the transplants.

The treated DLB mice showed significant improvements in both motor and cognitive function, note the authors. For example, they could recognize new objects more readily and they could run on a rotating rod for much longer than untreated DLB mice.

On further investigation, the team found that the stem cells enhanced two brain features that become dysfunctional in DLB. These features are neurons that produce the chemical messengers dopamine and glutamate. The researchers found that the stem cells produced a growth factor called brain-derived neurotrophic factor (BDNF) that enhanced the function of these dopamine and glutamate-producing neurons.

Enhancing the function of these neurons coaxes brain cells in the regions affected by DLB to connect and communicate better, and this, in turn, results in improved motor and cognitive function.

BDNF plays a critical role, but does not work so well on its own

To verify that it was the BDNF in the stem cells that led to the improvements, the team carried out the experiments again using stem cells that could not produce BDNF. When they transplanted them into the DLB mice, they found the BDNF-deficient stem cells did not improve behavioral function nor enhance dopamine and glutamate signaling.

Using a virus to deliver the growth factor into the brains of DLB mice, the team then ran a final set of experiments to see if BDNF alone could affect the improvements. This led to good recovery of motor function but limited improvement in cognitive function.

The researchers conclude that while BDNF appears to play a critical role, it cannot do it on its own - it has to work through the stem cells to result in improvements in both cognitive and motor function.

While the team is hopeful that one day DLB will be treatable by transplantation of BDNF-producing neural stem cells, they acknowledge there is still a long way to go and a lot of hurdles to overcome, as Mathew Blurton-Jones, an associate professor of neurobiology and behavior who led the UCI team, explains:

"Many important questions remain before we could envision moving forward with early-stage trials. For example, we'll need to identify and test human neural stem cells first."

However, should the approach overcome all these hurdles, then there is also the potential of using it to develop treatments for other neurodegenerative diseases that involve BDNF, dopamine and glutamate, such as **Huntington's disease** and Alzheimer's.

The study follows another successful mouse study that *Medical News Today* reported earlier this year that raises the hope that one day; **stem cell therapy for liver failure could replace liver transplants**. Writing in the journal *Nature Cell Biology*, the researchers describe how they restored organ function in severely damaged livers in mice by transplanting lab-grown stem cells.

Written by **Catharine Paddock PhD**