International research identifies a new way to enhance myelin repair in the brain

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MS results from the loss of myelin, the insulating coating of nerve fibres, in the brain and spinal cord. Lost myelin can be replaced and repaired naturally by stem cells that are present in the brain. This process of remyelination is how some people with MS are able to recover physical functions after a relapse. However, this process of repair is often incomplete, leading to the eventual progression of disease in many people with MS.

Enhancing or improving this natural repair process is one avenue for the discovery of new treatment options for existing damage in MS.

New research from New York University, published in the prestigious journal *Nature*, has identified that blocking a molecule in the stem cells in the brain successfully improves the stem cells' ability to repair damaged myelin.
Two types of brain stem cells can remyelinate nerve fibres – oligodendrocyte progenitor cells and neural stem cells. The researchers concentrated on one subset of neural stem cells that carried a molecule known as Gli1. These stem cells are involved specifically in restoring damaged myelin in the adult brain and spinal cord.

The researchers first tested the stem cells in mouse models where myelin had been damaged using a toxin. They showed that the Gil1 neural stem cells were able to move into areas of damaged myelin and restore lost myelin. They noticed that at the final stage of the repair process the Gli1 molecule was reduced. This prompted the researchers to test what would happen if the Gli1 molecule was blocked completely. Remarkably, they showed that the myelin repair process was significantly improved when the Gli1 molecule was genetically blocked in the stem cells.

In another series of experiments, when Gli1 was blocked using a drug given either orally or by injection into the mice, further increased levels of myelin repair was seen. The use of the drug did not affect myelin repair being carried out by other types of stem cells (such as oligodendrocyte progenitor cells) so the increase in myelin repair by the Gli1-blocked neural stem cells was in addition to other remyelination processes.

The final set of experiments used a mouse model where myelin is damaged by inflammation, a model which more closely resembles the human form of MS. When Gli1 was blocked by a drug in these experiments, the relapses were less severe and the recovery of function after the relapse was better. Mice who received the drug also had higher overall levels of myelin, less damage to nerve fibres and the number of

nerve cells in the spinal cord were higher, suggesting that blocking Gli1 protects nerve cells from damage as well as promoting myelin repair.

While much work remains to be done to see if modulating Gli1 in human stem cells can promote myelin repair, these exciting results have uncovered a potentially new approach for treating damage in MS.