

Harnessing the brain's own ability for repair

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New findings throw light on how the brain heals itself and may change the way we think about treating chronic neurodegenerative diseases like Parkinson's and Alzheimer's.

Neuroscientists at Sydney's Garvan Institute of Medical Research have shown that nerve cells in the brain produce an anti-inflammatory molecule that allows the brain to repair itself.

These findings, by Drs Bryce Vissel and Andrea Abdipranoto, are published online today in the international journal *Stem Cells*.

Discovery of the brain's capacity to regenerate is very recent. Neural stem cells were first discovered in the brain in the early 1990s, but it took scientists a further 10 years to show that they can regenerate nerve cells in the brain.

"Given that we now know regeneration can occur, we want to understand what drives it and what blocks it, particularly in diseases like Parkinson's and Alzheimer's." said Dr Vissel.

"We triggered rapid neurodegeneration in the brains of mice, and it was immediately followed by a very rapid regenerative response. We wanted to know why this response could occur so effectively after acute neurodegeneration.

"On further investigation, we found high levels of a molecule known as Activin A whenever regeneration occurred. This was especially interesting because Activin A is released from nerve cells.

"Clearly Activin A was playing an important part in the regenerative process, so we triggered neurodegeneration and at the same time blocked Activin A. The difference was dramatic. Regeneration all but ground to a halt."

"After these initial experiments, we thought that nerve cells may directly drive regeneration by releasing Activin A. We came to realise, however, that the main action of Activin A was to block inflammation in the brain after neurodegeneration or injury."

"We confirmed this by introducing another anti-inflammatory molecule, while continuing to block Activin A. As anticipated, the substituted anti-inflammatory allowed regeneration to occur."

"Inflammation is the body's way of trying to clear up a mess. We've shown that, if uncontrolled, it seems to be the very thing that can prevent regeneration and prevent healing of the brain."

Having done this study in a model of acute degeneration, the group is now doing the same work in chronic degenerative models.

It is likely that inflammation aggravates existing damage in the central nervous system of people with Parkinson's, Alzheimer's and motor neuron disease. Vissel and colleagues believe that chronic inflammation is probably providing a harmful feedback loop, preventing regeneration and contributing to progressive decline.

"Clearly the brain's anti-inflammatory response is not working well in chronic neurodegenerative diseases," said Vissel.

"There are a number of studies showing that people who take non-steroidal anti-inflammatory drugs have a lower risk of Alzheimer's and Parkinson's disease."

Should the group confirm that inflammation is blocking regeneration in Parkinson's, Alzheimer's and motor neuron disease, Activin A and derivatives need to be investigated as potential therapeutics.

NOTE TO EDITORS

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ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with nearly 500 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Osteoporosis and Bone Biology, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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