Researchers crack degeneration process that leads to Alzheimer's

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A research group led by Dr. A. Claudio Cuello of McGill University's Faculty of Medicine, Dept. of Pharmacology and Therapeutics, has uncovered a critical process in understanding the degeneration of brain cells sensitive to Alzheimer's disease (AD). The study, published in the February issue of the *Journal of Neuroscience*, suggests that this discovery could help develop alternative AD therapies.

A breakdown in communication between the brain's neurons is thought to contribute to the memory loss and cognitive failure seen in people with AD. The likely suspect is NGF (Nerve Growth Factor), a molecule responsible for generating signals that maintain healthy cholinergic neurons – a subset of brain cells that are particularly sensitive to AD – throughout a person's lifetime. Oddly, scientists had never been able to find anything wrong with this molecule to explain the degeneration of cholinergic neurons in patients with AD.

This new study, however, has elucidated the process by which NGF is released in the brain, matures to an active form and is ultimately degraded. The researchers were also able to determine how this process is altered in AD. The group demonstrated that treatment of healthy adult rats with a drug that blocks the maturation of active NGF leads to AD-like losses of cholinergic functional units, which result in cognitive impairments. By contrast, when treated with a drug to prevent degradation of active NGF, the numbers of cholinergic contacts increased significantly.

"Part of the difficulty in understanding this pathway has been due to the technical challenges associated with differentiating the active and inactive forms of NGF," explained Dr. Simon Allard, the study's lead author and a postdoctoral fellow at McGill. "Our proposed manipulations are different from existing therapies as they aim to protect neurons from degeneration."

The authors suggest that these findings may lead to pharmacological treatments that could delay the progression of Alzheimer's disease. "This discovery should help design alternative therapies," said Dr. Cuello, a Charles E. Frosst / Merck Chair.

Provided by McGill University