Impaired recovery from inflammation linked to Alzheimer's disease

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(Medical Xpress)—New research from Karolinska Institutet shows that the final stage of the normal inflammatory process may be disrupted in patients with Alzheimer's disease. A study published in the journal Alzheimer's & Dementia shows that levels in the brain and cerebrospinal fluid of the molecules necessary for tissue recovery through the clearance of harmful inflammatory substances are lower than normal in patients with Alzheimer's disease. The study also showed association between the lower levels of these molecules with impaired memory function.

Alzheimer's disease is the most common form of dementia, eventually leading to neuronal death associated with an increasing degree of memory impairment. As with other neurodegenerative diseases, Alzheimer's is characterised by an inflammatory process in the brain. Prolonged inflammation with the release of inflammatory and toxic substances can cause further damage and neuronal death. The inflammatory process normally ends in what is known as resolution. This is an active process regulated by certain molecules, so called specialized pro-resolving mediators, where the tissue is cleared from microorganisms, debris from dead cells via an uptake mechanism (phagocytosis), and where the release of growth factors stimulates tissue repair.

Together with colleagues in the United States, researchers at Karolinska Institutet have now shown that the levels of resolution-regulating molecules in the brain and in the cerebrospinal fluid are lower in

Alzheimer's disease than normal. The researchers have also shown that the lower levels of these molecules correlate with a lower degree of cognitive function, that is, memory capacity. The results are based on analyses of cerebrospinal fluid from 15 patients with Alzheimer's disease, 20 patients with mild cognitive impairment and 21 control subjects. The researchers also analysed brain tissue from 10 Alzheimer's patients and 10 control subjects.

"Our hypothesis is that stimulation of resolution of inflammation in Alzheimer's disease may result in reduced neuronal death in the brain, and in turn have a beneficial effect in disease progression and cognition. This is an entirely new approach and provides the opportunity to develop new treatment principles for Alzheimer's disease," says Professor Marianne Schultzberg, who led the study at the Department of Neurobiology, Care Sciences and Society.

In ongoing studies, the researchers are now investigating how the pro-resolving molecules affect neuronal death in cell cultures, and whether treatment in animal experiments with these substances can prevent neurodegeneration and improve memory functions. The pro-resolving molecules identified so far are derivatives of omega-3 fatty acids, which constitute a popular food supple-ment that has been ascribed several health benefits, and have received attention for beneficial effects also on factors related to Alzheimer's disease, in line with the new results described above. In previous studies, the researchers behind these new findings have shown that omega-3 also stimulates cells to take up amyloid-beta, a protein that kills neurons and occurs in the brain in the form of plaques in Alzheimer's disease.

More information: Resolution of inflammation is altered in Alzheimer's disease, *Alzheimer's & Dementia*, online 14 February 2014. The paper is available here: www.alzheimersanddementia.com/ … (14)00030-2/abstract

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