Stress may increase risk for Alzheimer's disease

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Stress promotes neuropathological changes that are also seen in Alzheimer's disease. Scientists from the Max Planck Institute of Psychiatry in Munich have discovered that the increased release of stress hormones in rats leads to generation of abnormally phosphorylated tau protein in the brain and ultimately, memory loss.

Protein deposits in nerve cells are a typical feature of Alzheimer's disease: the excessive alteration of the tau protein through the addition of phosphate groups – a process known as hyperphosphorylation – causes the protein in the cells to aggregate into clumps. As a result, nerve cells die, particularly in the hippocampus, a part of the brain that plays an important role in learning and memory, as well as in the prefrontal cortex which regulates higher cognitive functions.

Fewer than ten percent of Alzheimer cases have a genetic basis. The factors that contribute to the rest of the cases are largely unknown. Following up on epidemiological studies, scientists at the Max Planck Institute of Psychiatry hypothesized that adverse life events (stress) may be one trigger of Alzheimer's disease.

In cooperation with colleagues at the University of Minho in Braga, Portugal, the Munich-based researchers have now shown that stress, and the hormones released during stress, can accelerate the development of Alzheimer disease-like biochemical and behavioural pathology. They found increased hyperphosphorylation of tau protein in the hippocampus and prefrontal cortex of rats that has been subjected to stress (e.g.

overcrowding, placement on a vibrating platform) for one hour daily over a period of one month. Animals showing these changes in tau also showed deficits in memories that depended on an intact hippocampus; also, animals with abnormally hyperphosphorylated tau were impaired in behavioural flexibility, a function that requires proper functioning of the prefrontal cortex.

These results complement previous demonstrations by the scientists that stress leads to the formation of beta-amyloid, another protein implicated in Alzheimer's disease. "Our findings show that stress hormones and stress can cause changes in the tau protein like those that arise in Alzheimer's disease", explains Osborne Almeida from the Max Planck Institute of Psychiatry.

The next challenge will be to see how applicable the results obtained in animals are to the development of non-familial forms of Alzheimer's disease. "Viewing stress as a trigger of Alzheimer's disease offers exciting new research possibilities aimed at preventing and delaying this severe disease. Moreover, since vulnerability to major depression is known to be increased by stress, it will be interesting to know the role of molecules such as beta-amyloid and tau in the onset and progress of this condition", says Osborne Almeida.

More information: Ioannis Sotiropoulos, Caterina Catania, Lucilia G. Pinto, Rui Silva, G. Elizabeth Pollerberg, Akihiko Takashima, Nuno Sousa, and Osborne F. X. Almeida, Stress Acts Cumulatively to Precipitate Alzheimer's Disease-Like Tau Pathology and Cognitive Deficits, *Journal of Neuroscience*, May 25, 2011; 31(21):7840-7847

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