Researchers discover misfolded protein clumps common to dementia, Lou Gehrig's disease

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Scientists have identified a misfolded, or incorrectly formed, protein common to two devastating neurological diseases, frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease), according to a report in the Oct. 6, 2006, issue of *Science*. The findings suggest that certain forms of FTD, ALS and possibly other neurological diseases might share a common pathological process.

Virginia Lee, Ph.D., and John Trojanowski, M.D., Ph.D., of the University of Pennsylvania, led an international team of scientists in this discovery. The work was funded by the National Institute on Aging (NIA), part of the National Institutes of Health (NIH), and was done at the NIA-funded Alzheimer's Disease Center at the University of Pennsylvania School of Medicine Institute on Aging.

"This exciting basic science discovery provides the first molecular link between a dementia--FTD--and a motor neuron disease--ALS. It will advance understanding of the pathological processes of FTD and ALS, and possibly of other neurological disorders," says NIA director Richard J. Hodes, M.D. Improved understanding of underlying disease processes is critically important in pointing researchers toward the development of therapies for FTD, ALS and other neurodegenerative diseases, Hodes and the study authors note.

FTD affects the frontal and temporal lobes of the brain. People with FTD may exhibit uninhibited and socially inappropriate behavior, changes in personality and, in late stages, loss of memory, motor skills and speech. After Alzheimer's disease, it is the most common cause of dementia in people under age 65.

ALS is a progressive disease of brain and spinal cord motor neurons that control movement. Over time, walking, eating, speaking and breathing become more difficult in this fatal disease. Some people with ALS also have FTD, and some with FTD also develop ALS, suggesting that common mechanisms might underlie these two diseases.

In certain neurodegenerative diseases, including ALS and some forms of FTD, scientists have identified clumps of protein--or inclusion bodies--that accumulate in brain cells and neurons. However, understanding why they form and what they contain has been elusive. Lee and Trojanowski have long sought to solve that mystery.

Following years of research, they have now identified TDP-43 as a constituent part of the clumps that form in ALS and in the most common form of FTD. Although its precise role is not well understood, TDP-43 is involved in the complex process of transcribing and regulating genetic information in the nucleus of the cell.

"There is much more to learn about how this nuclear protein is clumped in the cytoplasm of cells and about the mechanism by which it is implicated in two distinctly different diseases," says Stephen Snyder, Ph.D., program director, etiology of Alzheimer's disease, NIA Neuroscience and Neuropsychology of Aging Program. "It is possible that the TDP-43 protein will be a key to a more complete understanding of both FTD and ALS."

Source: National Institute on Aging