Neuroimaging study describes Alzheimer's disease-like changes in elderly people without the disease

March 15 2010

The emergence of multiple new brain imaging technologies and the combined application of these new approaches is helping to create new insights into aging and Alzheimer's disease. One of the hallmarks of Alzheimer's disease is the deposition of amyloid beta protein in clumps or "plaques" within the brain. These plaques can be measured in humans with PET scans that use a chemical marker or radiotracer called 11C-PIB.

It was long thought that the formation of plaques injured and perhaps even caused the death of nerve cells in the brain. Recent studies, however, suggest that a form of the amyloid beta protein that is soluble rather than the form that is deposited in plaques mediates most of the destructive impact of this protein.

In a new study published in *Biological Psychiatry* researchers have related the findings that are emerging from PET-PIB imaging to changes in the function of brain circuits. Sheline and colleagues examined Alzheimer's disease patients and cognitively normal, healthy individuals who were then divided into those with or without brain amyloid plaques.

Using functional connectivity brain mapping, they found that amyloid plaques are present in the brains of people with Alzheimer's disease as well as some healthy elderly people who do not show behavioral evidence of Alzheimer's disease. However, they found that the healthy

participants with brain amyloid deposits were associated with compromise of the connections between important brain regions involved in learning and memory even though their memory functions were not markedly impaired. Similar disruptions in brain connections were found in individuals with Alzheimer's disease.

"This elegant study illustrates that amyloid plaques are only a component of the disease process in Alzheimer's disease, in that that there are many people who have the plaques but not the disease. These data raise a number of important questions," comments Dr. John Krystal, Editor of Biological Psychiatry. "What is missing from the disease process or what protective factors are present among people who have amyloid deposition in plaques but who appear to be without Alzheimer's disease? If the amyloid plaques were eliminated in the healthy elderly, would their brain circuitry function normalize?"

These questions are important and timely as a number of approaches for reducing brain amyloid beta protein levels are currently being tested, including antibodies that might bind to and promote the clearance of amyloid beta protein as well as drugs that inhibit amyloid beta protein synthesis. If amyloid beta protein is only part of the biology of Alzheimer's disease, it may be difficult to predict the extent to which these novel treatments might work.

According to Dr. Yvette Sheline, Professor of Psychiatry and Radiology at Washington University and lead author on the study, "the important thing about this study is that none of the participants had cognitive or behavioral abnormalities. This indicates that Alzheimer's disease likely begins quietly, clinically undetected, but still slowly eroding brain networks." Thus, these findings further underscore the importance of being able to identify individuals at risk for developing Alzheimer's disease, and will aid researchers as they continue to work to understand the disruption in brain functioning associated with Alzheimer's disease.

More information: The article is "Amyloid Plaques Disrupt Resting State Default Mode Network Connectivity in Cognitively Normal Elderly" by Yvette I. Sheline, Marcus E. Raichle, Abraham Z. Snyder, John C. Morris, Denise Head, Suzhi Wang, and Mark A. Mintun. The authors are affiliated with the Washington University School of Medicine, St. Louis, Missouri. The article appears in *Biological Psychiatry*, Volume 67, Issue 6 (March 15, 2010)

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