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Tissue-Specific Protein Clusters May Help Predict Risk of Alzheimer's Disease

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Alzheimer's disease is the most prevalent form of dementia, characterized by the aggregation of amyloid beta and tau proteins which form plaques and neurofibrillary tangles. The assembly of these amyloid plaques and tangles across specific brain tissues follows a characteristic pattern that has led to neuropathological staging for Alzheimer-related changes. But the reasons why some brain tissues are more selectively vulnerable than others to plaque formation, and whether this vulnerability could be detected before symptoms even develop, remain unknown.

A study published online in the August 10th, 2016 issue of the journal *Science Advances* investigated whether the cell environments of the most vulnerable brain tissues are predisposed in some way to protein aggregation and subsequent plaque formation, possibly due to failures in protein homeostasis within those tissues. If this were true, could this lead to the production of a vulnerability map of healthy brains?

The research team from the University of Cambridge analyzed data from six healthy human brains of individuals ages 24 to 57. Tissue samples, derived from the Allen Brain Atlas, were taken from more than 500 regions for each hemisphere as part of a transcriptome-wide microarray analysis. The analysis revealed elevated mRNA expression levels of proteins that form plaques and tangles in the tissues where Alzheimer's disease first becomes evident. Likewise, components of the brain's protein homeostasis system, which protect against amyloid beta and tau aggregation, had lower mRNA expression levels in tissues known to be vulnerable to Alzheimer's disease. This combination of higher plaque-forming protein expression with lower plaque-controlling protein expression became the study's predictive tool for tissue vulnerability to Alzheimer's, and the regions where these vulnerability patterns emerged paralleled the known staging of the disease.

The study concluded that the susceptibility of specific tissues to plaque formation is a feature of healthy brains, and that the particular expression signature associated with protein aggregation could potentially be observed in the form of a vulnerability map decades before the typical age of onset for Alzheimer's disease. The authors suggest that this could one day open the possibility of identifying individuals at risk for Alzheimer's long before symptoms appear.

This has been a presentation of AudioAbstracts. For more information, and for reference links to this article in the journal *Science Advances*, visit ReachMD.com.