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UNTIL SUNDAY, JULY 17, 2011, 7:00 AM CEST (1:00 AM ET/USA)

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**FALLS MAY INDICATE EARLIEST STAGES OF ALZHEIMER'S AND
NEED FOR FURTHER EVALUATION**

- Also, Preliminary Results on a Possible New "Eye Test" for Alzheimer's -

PARIS, July 17, 2011 – Falls are more common among individuals with the earliest signs of Alzheimer's, according to a study presented at the Alzheimer's Association International Conference 2011 (AAIC 2011). The study measured the rate of falls among cognitively healthy older adults with and without preclinical Alzheimer's – as measured by amyloid imaging using positron emission tomography (PET) with Pittsburgh compound B (PiB) – and found twice the risk of falls for people with higher levels of PiB on their scan.

In older adults, falls contribute to increased disability, premature nursing home placement and injury-related mortality. There are also higher health care costs associated with falls – more than \$19 billion could be attributed to the direct medical costs of falls in 2000. Older adults with Alzheimer's may be at higher risk for falls because of balance and gait disorders and problems with visual and spatial perception that are caused by the disease.

“Understanding the traditional hallmarks of Alzheimer's, including cognitive impairment and memory loss, are important; however, these study results also illustrate the significance of understanding that, in some people, changes in gait and balance may appear before cognitive impairment,” said Maria Carrillo, PhD, Alzheimer's Association Senior Director of Medical and Scientific Relations.

“Growing scientific evidence suggests that ‘silent’ biological changes may be occurring in the brain a decade or more before we can see the outward symptoms of Alzheimer's. According to this study, a fall by an older adult who otherwise has a low risk of falling may signal a need for diagnostic evaluation for Alzheimer's,” continued Carrillo.

Led by Susan Stark, PhD, Assistant Professor of Occupational Therapy and Neurology at Washington University in St. Louis, the 8-month study followed 125 older adults currently enrolled in longitudinal studies of memory and aging at Washington University's federally funded Knight Alzheimer's Disease Research Center (ADRC). All participants had PiB PET imaging and contributed samples of cerebrospinal fluid (CSF). Each participant was asked to record in a journal how many times they experienced a fall, which was defined as unintentional movement to the floor,

ground or an object below knee level. Some of participants had preclinical Alzheimer's and some did not. With an average of 191 days of data collected for participants, the study found that 48 people experienced at least one fall. A positive PiB PET image resulted in a 2.7 times greater risk of a fall for each unit of increase on their PiB PET scan.

“To our knowledge, this is the first study to identify a risk of increased falls related to a diagnosis of preclinical Alzheimer's disease,” said Stark. “This finding is consistent with previous studies of mobility problems among persons with very early symptomatic Alzheimer's or mild cognitive impairment. It suggests that higher rates of falls can occur very early in the disease process.”

“In the near future, with continued research, we will improve our ability to detect and intervene early in Alzheimer's disease. With earlier detection, perhaps we can also lower the risk of falls, which can be disabling, expensive and even deadly in older adults,” said Carrillo. “Additional research is urgently needed, for example to further explore the connection between motor deficits and falls as possible early signals of Alzheimer's.”

Retinal Imaging May Prove Useful In Identifying Individuals at Risk for Alzheimer's

Another study featured at AAIC 2011 explored whether characteristics of blood vessels in the retina (the light-sensitive layer at the back of the eye) might serve as possible biomarkers for Alzheimer's disease. While most Alzheimer's-related pathology occurs in the brain, the disease has also been reported to create changes in the eye, which is closely connected to the brain, and more easily accessible for examination in a doctor's office.

“Today, there is no single method for detecting Alzheimer's until the disease is well advanced. Current PET and MRI scans can detect some brain changes, but these procedures can be expensive and technically challenging, and so are impractical for testing in large populations,” said Shaun Frost, MSc, of CSIRO's Australian e-Health Research Center.

In a small pilot study, Frost and colleagues examined retinal photographs of people with Alzheimer's (n=13), mild cognitive impairment (n=13) and healthy participants (n=110) from the larger Australian Imaging, Biomarker and Lifestyle (AIBL) Flagship Study of Ageing. They examined a variety of parameters, including the width of retinal blood vessels.

They found that the width of certain blood vessels in the back of the eye were significantly different for people with Alzheimer's vs. healthy controls, and that this correlated with a brain imaging benchmark indicative of Alzheimer's disease – the deposition of amyloid plaque in the brain as measured by PET PiB imaging.

“Our studies are very preliminary, but encouraging,” said Frost. “Since amyloid plaque build up in the brain occurs years before cognitive symptoms of Alzheimer's are evident, a non-invasive and cost-effective retinal test may hold promise as an early detection tool for the disease. We hope that, in the future, our measure could be used with blood-based tests to help doctors identify who needs further assessment with PET imaging and MRI for Alzheimer's, but more research is needed.”

About AAIC

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

About the Alzheimer's Association

The Alzheimer's Association is the leading voluntary health organization in Alzheimer care, support and research. Our mission is to eliminate Alzheimer's through the advancement of research, to provide and enhance care and support for all affected, and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. Visit www.alz.org or call 800-272-3900.

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- Susan Stark, PhD, et al. Risk of falls among older adults with Preclinical Alzheimer's Disease. (Fundors: U.S. National Institute on Aging, the Knight Alzheimer's Disease Research Center at Washington University).
- Shaun Frost, MSc, et al. Retinal Vascular Parameters as Biomarkers for Alzheimer's Disease. (Fundors: Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australian e-Health Research Centre, Preventative Health Flagship, McCusker Alzheimer's Research Foundation, The Science and Industry Endowment Fund)

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Session: Sunday, July 17, 2011 Posters

Presentation: P1-201; 12:30-3:00 pm

Risk of falls among older adults with Preclinical Alzheimer's Disease

Presenting author: Susan Stark, PhD, Washington University, St. Louis, Missouri

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Background: Falls are the leading cause of disability and injury-related mortality among older adults. Balance and gait disorders are prevalent in persons with Alzheimer's disease (AD). To explore whether motor changes precede cognitive changes in persons who ultimately develop symptomatic AD, we examined the rate of falls among healthy older adults with and without preclinical AD based on their PIB PET imaging studies and molecular biomarker profile.

Methods: We conducted a 5-month prospective cohort study to examine the cumulative incidence of falls among 114 community-dwelling cognitively normal older adults. Participants were evaluated clinically and had PIB PET imaging and assays of cerebrospinal fluid (CSF).

Falls (unintentional movement to the floor, the ground, or an object below knee level) were reported monthly using an individualized calendar-journal returned by mail. Participants with a mean cortical binding potential (MCP) of <0.18 were considered negative or without substantial brain amyloid plaque burden based on their PIB PET study.

A Cox proportional hazards model was used to test whether time to first fall was associated with MCP at baseline, after adjustment for age, gender, education, and race. Similar analyses were conducted for each of the CSF biomarkers and the ratio of tau/A β 42 and ptau/A β 42. Kaplan-Meier survival curves were constructed for the PIB groups and for each molecular biomarker.

Results: The sample was predominately female (63.9%) and white with a mean age of 74.5 years. The response rate was 100% with an average of 100 days of data available. There were 33 participants who experienced a fall.

With the exception of CSF A β 42, higher levels of each biomarker were associated with a faster time to first fall. A positive PIB PET image resulted in a 5.36 times greater chance of experiencing a fall among healthy older adults.

Conclusions: Preclinical AD is a risk factor for falls in older adults. This study points to the importance of understanding not only the cognitive impairments associated with AD, but also the motor changes that appear to precede cognitive changes. Additional research is needed to assess the extent of fall risk among healthy older adults with preclinical AD.

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Session: Sunday, July 17, 2011 Posters

Presentation: P1-081; 12:30-3:00 pm

Retinal Vascular Parameters as Biomarkers for Alzheimer's Disease

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Background: A screening process that could provide early, accurate diagnosis or prognosis for AD would enable current and future treatments to be more effective, as well as contribute to the development of new treatments through better defined cohorts and earlier intervention. While most AD related pathology occurs in the brain, the disease has also been reported to affect the eye, which is more accessible for imaging than the brain. This preliminary report presents results from analysis of retinal photographs from AD, MCI and HC participants from the Australian Imaging, Biomarker and Lifestyle (AIBL) Flagship Study of Ageing and other research cohorts at the McCusker Foundation for Alzheimer's Disease Research in Perth, Australia.

Methods: Retinal photographs were collected and analysed with semi-automated software to calculate parameters such as the width of retinal vessels. Central retinal arterial (CRAET) and venular (CRVET) equivalent thickness and arterio-venular ratio (AVR) were calculated for each participant as per standardised methods. Retinal parameters were statistically analysed with respect to clinical status and neuro-imaging data (reduced cohort), adjusting for potential confounders.

Results: Significant differences in retinal AVR between AD and MCI ($p < 0.05$) and AD and HC ($p < 0.01$) groups ($n_{AD}=6, n_{MCI}=9, n_{HC}=90$) were observed. Changes to CRAET were not significant but CRVET was significantly different between AD and HC ($p < 0.02$). AVR and neocortical plaque-load were significantly correlated (Standardised Uptake Value Ratio - SUVR from PET-PiB neuroimaging) for both HC ($R=0.53, p < 0.02, n_{MCI}=6$) and MCI groups ($R=0.823, p=0.044, n_{HC}=21$). Neuroanatomically, the strongest correlations were found between AVR and left-frontal SUVR (MCI: $R=0.90, p < 0.02$, HC: $R=0.58, p < 0.01$). For the MCI group ($n=6$) but not the HC group ($n=21$), retinal AVR was also correlated with Ventricle volume calculated from MRI images ($R=0.91, p < 0.02$). Data collection is continuing in February 2011.

Conclusions: These preliminary findings indicate a relationship between retinal vascular parameters, neocortical plaque load and AD. Since neocortical plaque load increases many years before the cognitive symptoms of AD arise, a non-invasive retinal test holds promise as an integral part of a screening test for early detection of AD.

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