Advances in brain imaging can expedite research and diagnosis in Alzheimer's disease

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Alzheimer's disease (AD) is a common problem that is becoming progressively burdensome throughout the world. A new supplement to the *Journal of Alzheimer's Disease*, Imaging the Alzheimer Brain, clearly shows that multiple imaging systems are now available to help understand, diagnose, and treat the disease.

"Alzheimer's disease is now seen as a continuum that is influenced by factors early in life, including genetics and education," according to Guest Editor J. Wesson Ashford, MD, PhD, Clinical Professor and Senior Research Scientist at the Stanford/VA Alzheimer Center, Palo Alto, CA. "Conceptualizing the continuum of AD with advanced imaging technology will provide a greater understanding of the disease, and help advance diagnosis and the quest for prevention and treatment."

The supplement features both reviews of the basic concepts of neuroimaging in the context of AD, the latest developments in imaging, and various discussions and perspectives of the problems of the field and promising directions. It provides in-depth insights into: pathology and pathophysiological bases of AD; structural and cerebral blood flow imaging; metabolism, amyloid plaques, and neurofibrillary tangles in vascular co-morbidity and AD; current advances in functional magnetic resonance imaging for detecting AD; electromagnetic brain mapping; diffusion tensor imaging; magnetic resonance spectroscopy; and longitudinal neuroimaging measures.

Investigators have used brain imaging to track some of the earliest

changes associated with the predisposition to AD. In their paper, "Alzheimer's Prevention Initiative: A Plan to Accelerate the Evaluation of Presymptomatic Treatments," a group of scientists proposes to evaluate investigational treatments in healthy people who, based on their age and genetic background, are at the highest imminent risk of developing symptomatic AD. "It currently takes too many average healthy people, too much money, and too many years to evaluate the range of promising presymptomatic treatments using clinical endpoints," says lead author Eric M. Raiman, of the Banner Alzheimer's Institute and the University of Arizona. The project will use brain imaging studies, cerebrospinal fluid biomarkers, and cognitive measures to evaluate AD-modifying treatments earlier than is otherwise possible and to determine the extent to which the treatment's brain imaging and other biomarker effects predict a clinical benefit, among other outcomes.

Dr. Ashford comments that "even when imaging data are not applied to the management of individual patients, these data have the potential to assist in evaluating other components of care and diagnosis. To the extent that imaging can more sensitively measure brain integrity than existing techniques, novel treatments may be discovered because beneficial effects of treatments are not detectable with other methods."

Two articles in the supplement offer intriguing insights into the relationship between cortical thinning and AD. In "Relationship Between CSF Biomarkers of Alzheimer's Disease and Rates of Regional Cortical Thinning in ADNI Data," investigators from the Department of Veterans Affairs Medical Center, San Francisco, the University of California and the Hospital of the University of Pennsylvania tested the association between rates of regional brain cortex thinning and reduced amyloid (Ab1-42) and higher tau concentrations. Using data from the Alzheimer's Disease Neuroimaging Initiative, they found that these biomarkers were associated with increased rates of brain tissue loss, and that the patterns varied across the healthy elderly and the mildly

cognitively impaired. "The finding of faster progression of brain atrophy in the presence of lower Ab1-42 levels and higher p-tau levels supports the hypothesis that they are measures of early AD pathology," says lead author Duygu Tosun.

It's known that the presence of an ApoE e4 (e4+) allele increases the risk of developing AD. There is an adverse relationship between e4+ status and brain structure and function in mild cognitive impairment; the presence of an e2 allele may be protective. In "Presence of ApoE e4 Allele Associated with Thinner Frontal Cortex in Middle Age," investigators examined whether the brain cortex thinning is the result of the disease, or a pre-existing endophenotype. Drawing on imaging data from a large national sample, the study examined the influence of ApoE on regional brain thickness and structure. The presence of the e4+ demonstrated significantly thinner cortex in the frontal areas, and may explain susceptibility to AD. The presence of the e2 allele was related to thicker cortex, suggesting a protective role.

In all, 31 papers discuss the advances in numerous imaging methodologies that are being used to increase our understanding of the pathophysiological basis of AD and drive us toward new therapies for this complex brain disorder. "Ultimately, the prospects for neuroimaging to enhance clinical care in Alzheimer's disease are bright as researchers collaborate and clinicians become informed about innovations and advances," says George Perry, PhD, Editor-in-Chief, Journal of Alzheimer's Disease, and Dean and Professor, College of Sciences, University of Texas at San Antonio.

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