Protein-based biomarkers in blood serum could classify individuals with Alzheimer's disease

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An initial analysis suggests that biomarkers in blood serum can be combined with clinical information to accurately classify patients with Alzheimer's disease, according to a report in the September issue of *Archives of Neurology*, one of the JAMA/Archives journals.

"There is clearly a need for reliable and valid diagnostic and prognostic biomarkers of Alzheimer's disease, and in recent years, there has been an explosive increase of effort aimed at identifying such markers," the authors write as background information in the article. "It has been previously argued that, because of significant advantages, the ideal biomarkers would be gleaned from peripheral blood." Identifying biomarkers in the blood has several advantages over other methods of classifying patients with Alzheimer's disease, including detecting biomarkers in the cerebrospinal fluid and neuroimaging. Blood can be collected at any clinic or in-home visit and most patients will agree to the process, whereas not all facilities can conduct lumbar punctures to obtain cerebrospinal fluid. Older patients may not consent to lumbar puncture and may not be able to undergo neuroimaging because of pacemakers or other health issues.

Sid E. O'Bryant, Ph.D., of Texas Tech University Health Sciences Center, Lubbock, and colleagues in the Texas Alzheimer's Research Consortium analyzed proteins in the serum of 197 patients diagnosed with Alzheimer's disease and 203 controls without Alzheimer's disease.

Statistical analyses were used to create a biomarker risk score, which included levels of a number of protein biomarkers, including fibrinogen (a clotting protein), interleukin-10 (associated with the immune system) and C-reactive protein (an inflammatory marker).

The final biomarker risk score correctly identified 80 percent of the individuals with Alzheimer's disease and accurately excluded 91 percent of the individuals without Alzheimer's disease. When other factors were also considered—age, sex, education and whether an individual had the APOE gene, which is associated with risk for Alzheimer's disease—the score correctly identified 94 percent of the individuals with Alzheimer's disease and accurately classified 84 percent of participants who did not have the disease.

"In addition to offering more accessible, rapid and cost- and time-effective methods for assessment, biomarkers (or panels of biomarkers) also hold great potential for the identification of endophenotypes within Alzheimer's disease populations that are associated with particular disease mechanisms," the authors write. In the current study, "a disproportionate number of inflammatory and vascular markers were weighted most heavily in the analyses." The findings provide support for the existence of an inflammatory subtype of Alzheimer's disease, they note.

"The identification of blood-based biomarker profiles with good diagnostic accuracy would have a profound impact worldwide and requires further validation," the authors conclude. "Additionally, the identification of pathway-specific endophenotypes among patients with Alzheimer's disease would likewise have implications for targeted therapeutics as well as understanding differential progression among diagnosed cases. With the rapidly evolving technology and the analytic techniques available, Alzheimer's disease researchers now have the tools to simultaneously analyze exponentially more information from a host of

modalities, which is likely going to be necessary to understand this very complex disease."

More information: Arch Neurol. 2010;67[9]:1077-1081.