Medical Xpress

Striatal brain volume predicts Huntington disease onset

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Huntington disease (HD) is an inherited neurodegenerative disorder caused by a defect on chromosome four where, within the Huntingtin gene, a CAG repeat occurs too many times. Most individuals begin experiencing symptoms in their 40s or 50s, but studies have shown that significant brain atrophy occurs several years prior to an official HD diagnosis. As a result, the field has sought a preventive treatment that could be administered prior to the development of actual symptoms that might delay the onset of illness.

Using data from the ongoing PREDICT-HD study and led by Dr. Elizabeth Aylward, author and Associate Director at the Center for Integrative Brain Research, Seattle Children's Research Institute, researchers examined whether neuroimaging measures can improve the accuracy of prediction of disease onset.

The PREDICT- HD study is an international, multi-site, long-term study of individuals who carry the gene mutation for Huntington disease but entered the study prior to onset of diagnosable motor impairment. Participants underwent structural magnetic resonance imaging (MRI) scans, which allowed for the comparison of individuals who developed HD during the course of the study and those who had not yet been diagnosed with HD.

They found that striatum and white matter volumes in the brain were significantly smaller in individuals diagnosed 1 to 4 years following the initial scan, suggesting that these volumetric measures can assist in

determining which individuals are closest to disease onset.

"We believe that the results of this study will be important in designing future clinical trials for individuals who have the Huntington disease gene mutation, but who are not yet showing symptoms. We also believe this group of individuals is well suited for drug intervention studies, as their brain involvement is not as severe as those who have already been diagnosed," said Dr. Aylward.

"Huntington disease can be considered a model neuropsychiatric disorder, since it is caused by a single gene and has such predictable and well-characterized brain changes. It may guide thinking about other disorders with genetic contribution, such as schizophrenia," commented Dr. Christopher A. Ross, co-author and Professor of Psychiatry, Neurology and Neuroscience, Johns Hopkins University. "If we could better understand the natural history of brain changes in schizophrenia, for instance, we may be able to identify genetically vulnerable individuals, and intervene therapeutically, not just to treat symptoms, but to alter the biology and course of the disease."

Dr. John Krystal, Editor of *Biological Psychiatry*, agreed, noting that "biomarkers of illness progress are critical for all neuropsychiatric disorders."

For now, these results may enhance the formulas used to calculate age of onset and help aid in the planning of future clinical trials aimed at delaying disease onset.

"Identifying individuals who are close to onset of diagnosable symptoms will allow feasible studies that use onset of symptoms as the primary outcome measure to determine if a drug intervention is effective," Dr. Aylward added. "Although it would be unreasonable to suggest that all potential clinical trial participants receive MRI scans one to four years

prior to taking part in a trial, there are many individuals who have participated in pre-HD observational studies who already have such data available."

Perhaps more importantly, Dr. Krystal concluded that "the development of good disease staging using MRI in Huntington disease could assist investigators studying novel treatments and affected individuals and family members anxious to learn about disease progress."

More information: The article is "Striatal Volume Contributes to the Prediction of Onset of Huntington Disease in Incident Cases" by Elizabeth H. Aylward, Dawei Liu, Peggy C. Nopoulos, Christopher A. Ross, Ronald K. Pierson, James A. Mills, Jeffrey D. Long, Jane S. Paulsen, and PREDICT-HD Investigators and Coordinators of the Huntington Study Group (doi: 10.1016/j.biopsych.2011.07.030). The article appears in *Biological Psychiatry*, Volume 71, Issue 9 (May 1, 2012).

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