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Research points to biomarker that could track Huntington's disease progression

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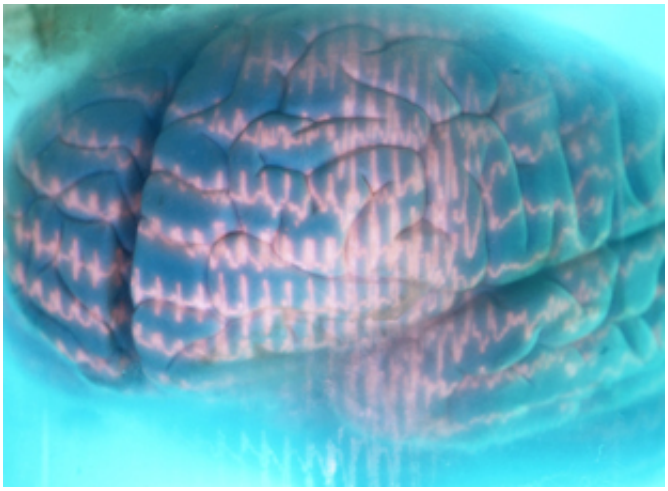

A hallmark of neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's is that by the time symptoms appear, significant brain damage has already occurred—and currently there are no treatments that can reverse it. A team of SRI International researchers has demonstrated that measurements of electrical activity in the brains of mouse models of Huntington's disease could indicate the presence of disease before the onset of major symptoms. The findings, "Longitudinal Analysis of the Electroencephalogram and Sleep Phenotype in the R6/2 Mouse Model of Huntington's Disease," are published in the July 2013 issue of the neurology journal *Brain*, published by Oxford University

Press.

SRI researchers led by Stephen Morairty, Ph.D., a director in the Center for Neuroscience in SRI Biosciences, and Simon Fisher, Ph.D., a postdoctoral fellow at SRI, used electroencephalography (EEG), a noninvasive method commonly used in humans, to measure changes in neuronal electrical activity in a mouse model of Huntington's disease. Identification of significant changes in the EEG prior to the onset of symptoms would add to evidence that the EEG can be used to identify biomarkers to screen for the presence of a neurodegenerative disease. Further research on such potential biomarkers might one day enable the tracking of disease progression in clinical trials and could facilitate drug development.

"EEG signals are composed of different frequency bands such as delta, theta and gamma, much as light is composed of different frequencies that result in the colors we call red, green and blue," explained Thomas Kilduff, Ph.D., senior director, Center for Neuroscience, SRI Biosciences. "Our research identified abnormalities in all three of these bands in Huntington's disease mice. Importantly, the activity in the theta and gamma bands slowed as the disease progressed, indicating that we may be tracking the underlying disease process."

EEG has shown promise as an indicator of underlying brain dysfunction in neurodegenerative diseases, which otherwise occurs surreptitiously until symptoms appear. Until now, most investigations of EEG in patients with neurodegenerative diseases and in animal models of neurodegenerative diseases have shown significant changes in EEG patterns only after disease symptoms occurred.

"Our breakthrough is that we have found an EEG signature that appears to be a biomarker for the presence of disease in this mouse model of Huntington's disease that can identify early changes in the brain prior to

the onset of behavioral symptoms," said Morairty, the paper's senior author. "While the current study focused on Huntington's disease, many neurodegenerative diseases produce changes in the EEG that are associated with the degenerative process. This is the first step in being able to use the EEG to predict both the presence and progression of neurodegenerative diseases."

Although previous studies have shown there are distinct and extensive changes in EEG patterns in Alzheimer's and Huntington's disease patients, researchers are looking for changes that may occur decades before disease onset.

Huntington's disease is an inherited disorder that causes certain nerve cells in the brain to die, resulting in motor dysfunction, cognitive decline and psychiatric symptoms. It is the only major neurodegenerative disease where the cause is known with certainty: a genetic mutation that produces a change in a protein that is toxic to neurons.

Provided by SRI International

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