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Study unveils unprecedented method to predict ALS, Parkinson's disease

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A new Mayo Clinic study details an unprecedented method to predict brain aging disorders such as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and Parkinson's disease. Investigators studied common variations within axon guidance pathway genes and identified several gene variations (DNA fingerprints) that collectively predicted people who are at a high risk for ALS (2,000 times greater than the average risk).

They also identified several gene variations that collectively predicted people at a high risk for Parkinson's disease (nearly 400 times greater than the average risk).

The probability that the findings were by chance was extremely small (less than one in a trillion). The axon guidance pathway consists of a complex array of chemical signals that wires the brain during fetal development and maintains and repairs brain wiring throughout life. The study is published online in the public access journal PLoS ONE.

"The mission of our research is to predict, prevent and halt brain aging disorders," explains Demetrius Maraganore, M.D., Mayo Clinic neurologist and principal investigator. "I envision a day when we will be able to do a simple blood test and predict whether a person is at high risk to develop brain aging disorders such as ALS, Parkinson's disease and even Alzheimer's disease by studying common gene variations in disease pathways. In persons at high risk, we may be able to prevent the diseases or slow or halt their progression by developing drugs that target the same

disease pathways. For ALS and Parkinson's disease, our study is a major step in these directions."

In June 2007, the investigators reported similar findings for Parkinson's disease. However, with this new study they extended their findings to ALS, where they observed greater effects. The investigators noted that while up to 50 percent of the axon guidance pathway genes that predict ALS or Parkinson's disease are in common, there also are gene variations that are specific to either disease. This may help explain the similarities and differences that are seen in persons with these diseases, or the clustering of such diseases that sometimes occur within isolated populations or families.

The investigators obtained these results by analyzing publicly available datasets of whole-genome variations in people with ALS, Parkinson's disease and those who did not have neurological disorders. The datasets were released recently by the Coriell Institute and the National Institutes of Health. The investigators developed and applied to the data a genomic pathways approach.

"The size of the effects that were observed and their statistical significance are unprecedented in the study of brain aging disorders. I attribute our success to the genomic pathways approach we developed," adds Timothy Lesnick, Mayo Clinic biostatistician. "Now we need to develop a better map of the gene variations within the axon guidance pathway and make comparisons across multiple brain aging diseases and populations."

ALS causes degeneration of the nerve cells in certain regions of the brain and spinal cord that control a person's voluntary muscles. Eric Sorenson, M.D., and Eric Ahlskog, M.D., Ph.D., Mayo Clinic neurologists specializing in ALS and movement disorders, agree that impairments in brain wiring and repair are plausible causes of ALS and

Parkinson’s disease. Investigators agree that additional research is needed to continue the success obtained in this study.

“I envision experiments in cultured cells and animal models to define the most important treatment targets within the axon guidance pathway,” says John Henley, Ph.D., Mayo Clinic neuroscientist and expert on brain wiring and repair processes.

Source: Mayo Clinic