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Study ties ABCC9 anomalies, sulfonylurea exposure to HS-Aging

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A genome-wide association study (GWAS) led by Peter Nelson, MD, PhD, of the Sanders-Brown Center on Aging at the University of Kentucky, and David Fardo, PhD, of UK's Department of Biostatistics, has provided new insight into Hippocampal Sclerosis of Aging (HS-A), a common disease affecting the elderly.

Researchers from 16 different institutions compared 363 persons with autopsy-proven HS-A to a control group of 2,303 other individuals in an attempt to identify genetic predisposition to HS-Aging.

Dr. Nelson and his team found that small changes in the ABCC9 gene—also known as Sulfonylurea Receptor 2—strongly paralleled the incidence of HS-Aging. Further statistical analysis demonstrated a link between the use of sulfonylurea, a medication commonly used to treat diabetes, and an increased risk for HS-A.

"This is the first genome-wide association study of its kind, and it has terrific statistical power," Dr. Nelson said. "While certainly there's a lot more work to be done to confirm the drug-disease interaction, this study nonetheless describes a novel dementia risk factor."

GWAS studies are a relatively new way to explore the linkage between any disease and the genetic factors that may contribute to them. Using the DNA of similar people with the target disease and without, millions of genetic variants are read and analyzed in an attempt to mark a region of the human genome that influences the risk of the target disease. In

contrast to methods which specifically test one or a few genetic regions, the GWA studies investigate the entire genome.

"This work confirms that the problems that occur in the brains of the elderly are complicated—but until we delve deeper into that complexity, we will be frustrated in our goal of finding new cures for these horrible diseases," Dr. Nelson said. "If further research confirms the genetic link we have identified in this study, it might inform new strategies to search for cures."

The Sanders-Brown Center on Aging is a worldwide leader in research on HS-A, a condition that affects up to 15% of individuals over age 85. Its symptoms are so similar to those of Alzheimer's disease that patients are often misdiagnosed with the latter. Currently, the only way to confirm a diagnosis of HS-A is by autopsy.

The study, which was funded in large part by the National Institute of Aging/National Institutes of Health, was published this week in *Acta Neuropathologica*.

Provided by University of Kentucky