Chemical from Soil Bacteria Shows Potential Neuron Toxicity; Has Possible Parkinson's Implications

October 6 2009

(PhysOrg.com) -- A chemical produced by common soil bacteria may kill neurons that produce dopamine, according to an article authored by University of Alabama researchers publishing Oct. 6. Dopamine neuron demise leads to the hallmark symptoms of Parkinson's disease, a movement disorder affecting some 1 million Americans.

The National Institutes of Health-sponsored research, publishing in the online open-access journal PLoS One, is preliminary, according to the UA scientists, but could shed light on those Parkinson's cases with no known genetic component - which are the vast majority. Environmental triggers have been linked to Parkinson's in previous studies.

"The data, so far, are seriously important, at best, and, at least, intriguing," said Dr. Guy Caldwell, associate professor of biological sciences at The University of Alabama, the NIH grant recipient and co-author of the research. "By no means do we feel this is anything of a conclusive nature, yet."

The research focuses on a chemical produced by a type of streptomyces, a bacterium frequently found in dirt and a top producer of antibiotics. This chemical, which the UA researchers say they believe is unknown to science, is likely produced by the bacteria as a secondary metabolite, said Dr. Julie Olson, an associate professor of biological sciences at UA and another co-author of the study.

Secondary metabolites are chemical compounds produced by organisms, including bacteria, often as a protective measure.

In laboratory experiments, the neurons which produce dopamine in worm animal models died when exposed to select strains of a bacterial culture containing the chemical.

“In general, the worms were fine, but the dopamine neurons started dying rapidly,” Caldwell said.

Further laboratory tests of the compound on human dopamine producing neurons, in collaboration with researchers at The University of Alabama at Birmingham led by Dr. David Standaert, director of the Center for Neurodegeneration and Experimental Therapeutics, showed it had a similar negative impact on the human neurons.

The tiny worms, a type of roundworm known as C. elegans, are acceptable animal models, much like lab rats, for studying various types of disease. Although simple and relatively inexpensive to work with, the worms have key neurotransmitters, like dopamine. More than 50 percent of all human hereditary diseases have been linked to genetic components also found in the worms. Three Nobel Prizes this decade have been awarded to worm researchers, including in 2008 to a C. elegans researcher who mentored Caldwell.

Lead author of the study is Dr. Kim A. Caldwell, associate professor of biological sciences at UA. Other UA authors include: Dr. Robert H. Findlay, professor of biological sciences, Dr. Tyler Hodges, a recent UA doctoral graduate, and students Michelle Tucci, Jafa Armagost, Jue Chen, Shermeen Memon, Jeana Blalock and Susan DeLeon.

The UA researchers said additional research is needed.

“Without having the compound purified, we don’t know whether or not the amounts people would be exposed to in a lifetime would be sufficient to cause problems,” said Olson. “It could be huge,” she said of the study’s implications. “It could be nothing. The jury is still out at this point.”

The UA research indicates the chemical may be causing the death of the dopamine producing neurons by disrupting a system that acts as cells’ “garbage disposal,” Caldwell said. This system, known as the ubiquitin proteasome system, or UPS, disposes of proteins which are misfolded or not functioning properly, and is linked to rare genetic forms of Parkinson’s.

“We have cellular evidence that this mechanism is being disrupted,” Caldwell said.

Left unchecked, one misfolding of a protein can lead to more and, eventually, cause an aggregation, or clumping, of proteins. This aggregation can lead to neuron malfunction or cell death.

The leading risk factor associated with Parkinson’s is aging. Living in rural areas, where lifestyle and occupational differences include drinking well water, farming and exposure to certain herbicides or pesticides, may increase, for some people, the risks of contracting the disease, the researchers said.

In addition to identifying the precise chemical involved, the UA researchers say they later hope to work with community members to take soil samples in parts of the state to see if they can isolate strains of streptomyces which produce the metabolites associated with the neurodegeneration.

Provided by University of Alabama