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MEETING ABSTRACTS

IDENTIFYING AXONAL TRANSPORT-RELATED TARGETS FOR REVERSING THE ADVERSE EFFECTS OF ORGANOPHOSPHATE EXPOSURE

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The chemicals known as the organophosphates (OPs) are found in hundreds of useful agricultural, industrial, and commercial products; however, they have also been associated with a variety of adverse health effects in humans and other non-target organisms. The acute toxicity of OPs is attributed to the inhibition of the enzyme acetylcholinesterase; however, this mechanism is inadequate to explain all of the long-term adverse effects of OPs. In both live imaging studies in primary neuronal culture as well as in manganese-enhanced magnetic resonance imaging (MEMRI) studies of the brains of living rats, we have observed impairments in axonal transport (AXT) associated with both the insecticide OP chlorpyrifos and the nerve agent OP diisopropylfluorophosphate. These observations may be important since AXT is an essential process that is responsible for the movement of a variety of important macromolecules to and from a neuron's cell body. In this presentation, a brief overview of the results of these neuronal culture (trafficking) and MEMRI experiments will be provided. In addition, the results of experiments conducted to date to identify specific molecular targets of OPs that might negatively influence axonal transport will be summarized. These targets include post-translational modifications of structural proteins that affect AXT through the regulation of microtubule dynamics and stability (e.g., Tau phosphorylation, Tubulin Acetylation), and specific signaling kinases (e.g., ERK GSKIIIβ) that are known to regulate various components of the AXT process. These experiments are expected to help us begin to develop novel therapeutic strategies to improve the neuronal deficits associated with OPs.

Keywords: Pesticide; Nerve Agent; Agriculture; Gulf War Illness

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