Apr 22nd, 10:00 AM - 4:00 PM

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TOWARDS AN UNDERSTANDING OF ALZHEIMER'S DISEASE II: THE VULNERABILITY HYPOTHESIS: DO GLUCOCORTICOIDS INCREASE CHOLINERGIC SUSCEPTIBILITY TO NEURAL TOXINS?

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Alzheimer's disease (AD) is a neurodegenerative disorder, currently affecting over 4 million Americans, with 100,000 new cases reported each year. AD is broadly characterized by a global and progressive deterioration of memory, cognition, and personality. The most evident clinical symptom of AD is memory loss. Studies in humans and rats report a significant correlation between this memory loss and a decline in cholinergic markers, such as choline acetyltransferase (ChAT) levels in the cerebral cortex and hippocampus. Therefore, one approach towad developing an animal model of AD is to induce lesions in the hippocampus. This was attempted in a number of studies, including one by Chrobak, Hanin, Schmechel, and Walsh (1988), in which lesioning of the hippocampus produced acetylcholine deficits, as measured by lower ChAT levels, which in turn produced behavioral deficits. Recently, it has been found that high concentrations of cortisol are linked to neuronal loss in AD. This postulate is a result of accumulating evidence suggesting that hypercortisolemia and a decreased negative feedback inhibition of cortisol secretion frequently accompany AD. In a recent study by Hortnagl, Berger, Havelec, and Hornykiewicz (1993) they reported that, when injected bilaterally into the lateral ventricles, the neurotoxin ethylcholine aziridinium (AF64A) induced specific reduction of ChAT activity throughout the hippocampus. In that same study, Hortnagl investigated the role of glucocorticoids in the cholinergic degeneration brought about by bilateral intracerebroventricular injections of AF64A (1 nmol/ventricle). They reported that chronic glucocorticoid administration seven days before surgery potentiates the susceptibility of cholinergic neurons to AF64A-induced deterioration. Though Hortnagl and colleagues explored the neurophysiological effects of glucocorticoid-potentiated AF64A toxicity, they did not explore the behavioral implications of these injections. Therefore, in the current study we investigated the effects of intracerebroventricular injections of AF64A on spatial learning in male rats chronically treated with glucocorticoids. Four groups were compared: group one, AF64A plus sesame oil; group two, AF64A plus corticosterone; group three, saline plus sesame oil; and group four, saline plus corticosterone. These groups were subjected to a visual discrimination task involving both a fixed and a floating platform in the Morris water maze. To assess the effects of the above injections, several parameters were measured: path length, swim speed, session latency, and choice errors. The results of this study will be presented at the conference.