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Toward an Understanding of Alzheimer's Disease VII: The Effects of βA (1-42) and Ibotenic Acid on the Retention of a Spatial Learning Task in Rats Following Multiple Injections into the Hippocampus

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TOWARD AN UNDERSTANDING OF ALZHEIMER'S DISEASE VII: THE EFFECTS OF ßA(1-42) AND IBOTENIC ACID ON THE RETENTION OF A SPATIAL LEARNING TASK IN RATS FOLLOWING MULTIPLE INJECTIONS INTO THE HIPPOCAMPUS

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Neuropathologically, Alzheimer's disease (AD) is characterized by neuritic plaques and neurofibrillary tangles. Evidence has suggested that a protein called ß-amyloid (ßA) is a major component of the neuritic plaques and may play a role in the neurodegeneration seen in AD. The cellular mechanisms by which ßA induces neurotoxicity, however, are still unclear. Recent evidence suggests that the aggregational state of ßA may be relevant to its neurotoxicity. Whether portions of the ßA protein or the entire sequence produces neurotoxicity in neurons, however, remains a controversy. Still another controversy is whether ßA is directly neurotoxic to neurons or whether it increases the vulnerability of neurons. Recent evidence reported by Dornan, Kang, McCampbell and Kang, that injections of ßA(25-35) with a low dose of ibotenic acid into the hippocampus did disrupt the acquisition of spatial learning in the rat, supports the vulnerability hypothesis. They suggest that the synergistic effect between ßA and ibotenic acid may have produced the neurotoxic effect. In light of recent evidence, reported at this conference, that injections of ßA(1-42) alone did not disrupt the retention of a spatial learning task, in this study we assessed the increased vulnerability hypothesis by coinjecting ßA(1-42) with a subthreshhold dose of ibotenic acid into the hippocampus of male rats. Another problem related to ßA's neurotoxicity may concern the extent of hippocampal damage it produces. Therefore, we will assess the effects of multiple injections of ßA(1-42) and ibotenic acid into the hippocampus of male rats. The results will be presented at the conference.