Apr 13th, 9:00 AM - 10:30 AM

# Cholinergic Immunolesions of the Medial Septal Area Using 192 IGG Saporin Induce a Differential Sensitivity of Muscarinic and Nicotinic Receptors on Spatial Learning in the Male Rat

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Poster Presentation 35

# CHOLINERGIC IMMUNOLESIONS OF THE MEDIAL SEPTAL AREA USING 192 IGG SAPORIN INDUCE A DIFFERENTIAL SENSITIVITY OF MUSCARINIC AND NICOTINIC RECEPTORS ON SPATIAL LEARNING IN THE MALE RAT

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Epidemiological studies indicate that the clinical entity known as Alzheimer's disease (AD) currently afflicts approximately 4 million people in the United States, with roughly 100,000 new cases diagnosed each year. This disorder typified by profound cognitive impairments, can also result in global personality changes as well. The most prominent feature of AD, particularly in the early stages, is memory loss. While significant progress has been made toward an understanding of the etiology of AD, presently no reliable animal model exists that mimics the profound pathological and behavioral changes that characterize the disease. A considerable amount of evidence has implicated the loss of cholinergic input to the hippocampus and cortex as being one of the major neuropathological components corresponding to the learning and memory deficits characteristic of AD. Therefore, one approach that this lab has taken toward the development of an animal model of AD is to mimic the loss of the cholinergic projection to the hippocampus and cortex using a variety of lesion techniques, and to determine how the loss of these fibers affect learning and memory in the rat. The most prominent cholinergic projection in the mammalian basal forebrain, is a projection from the medial septal area (MSA) to the hippocampus, in addition to a cortical projection that originates from the nucleus basalis magnocellularis (NBM). Collectively, these two areas account for approximately 80– 90 % of the cholinergic input to the hippocampus and cortex respectively. Considerable evidence suggests that, on the average, lesions of the MSA or NBM, induce substantial spatial learning impairments on both the Morris Water Maze, and radial arm maze. These impairments are associated with marked reductions in choline acetyltransferase (ChAT), which is an index of cholinergic activity. As a result, a cholinergic deficiency in the basal forebrain has been proposed to account for the cognitive deficits observed in AD. In this study we assessed the functional integrity of the cholinergic receptor system on spatial learning in animals that had received multiple injections of the immunotoxin 192–IgG saporin directly into the MSA. Our results reveal an increased sensitivity to muscarinic receptors but not nicotinic following 192 IgG saproin lesions of the MSA and further suggest a dissociation between the effects of muscarinic and nicotinic agents on spatial learning in rats. To our knowledge this is the first study that has examined the effects of muscarinic vs nicotinic agents in 192 IgG saporin lesioned animals. It is hoped that further research in this area will provide an avenue to test novel therapeutic drugs to be used as a palliative treatment for Alzheimer's disease.