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Alzheimer's disease currently afflicts approximately 4 million people in the United States, with 100,000 new cases being reported each year. This disorder is typified by several cognitive deficits, including memory loss. In our laboratory we have taken several approaches to the generation of a suitable animal model with which to study this disease. Previous work has focused on exploring a possible synergistic effect between a neurotoxic protein (beta amyloid) found in AD patients and stress. As post mortem examination of AD patients' brains has revealed a significant decrease in the number of cholinergic neurons, another approach we have taken is to look at the correlation between the depletion of certain cholinergic markers in animals and the resulting behavioral deficits. Two regions of specific interest are the medial septal area (MSA) and the nucleus basalis magnocellularis (NBM). These regions are important because they are the major source of cholinergic neurons in the brain, they are selectively targeted during aging and AD, and there have been many reports of their importance in learning and memory tasks. Earlier work has been done using the compound AF64A to selectively lesion cholinergic neurons, however, recent reports have brought into question the specificity of AF64A. Within the last few years a new chemical, saporin-IgG, has been introduced. The saporin-IgG complex (SIG) relies on the technique of immunolesioning, and initial reports show that it generates both very specific and complete lesions of cholinergic neurons. Therefore, for this study, rats have been injected with either the saporin-IgG complex or just the vehicle into either the medial septal area, or the nucleus basalis. One of the difficulties being reported while using SIG is the large percentage of animals that show signs of sickness and loss of motor skill after receiving intraventricular injections. This injection site is important, however, as it provides the most complete depletion of cholinergic markers in the brain. In order to avoid the deleterious effects on the animals health and still acquire the increase cholinergic depletion, one group of animals received injections into both the MSA and the NBM. The animals' behavior was assessed using a standard Morris' Water Maze task. After being trained for six days on a non-cued task, a probe trial was administered and the time spent in each quadrant was recorded.