INFORMATION TO USERS

This dissertation copy was prepared from a negative microfilm created and inspected by the school granting the degree. We are using this film without further inspection or change. If there are any questions about the content, please write directly to the school. The quality of this reproduction is heavily dependent upon the quality of the original material.

The following explanation of techniques is provided to help clarify notations which may appear on this reproduction.

1. Manuscripts may not always be complete. When it is not possible to obtain missing pages, a note appears to indicate this.

2. When copyrighted materials are removed from the manuscript, a note appears to indicate this.

3. Oversize materials (maps, drawings and charts are photographed by sectioning the original, beginning at the upper left hand corner and continuing from left to right in equal sections with small overlaps.

UMI®

ProQuest Information and Learning
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA
800-521-0600

MEMORY PERFORMANCE AND AGING: EXPERIMENTAL CHOLINERGIC TREATMENT

APPROVED:

Judith C. Goggin

Dean of the Graduate School

For Jim. . .

MEMORY PERFORMANCE AND AGING: EXPERIMENTAL CHOLINERGIC TREATMENT

by

SARA OLIVER ELLETT, B. S.

THESIS

Presented to the Faculty of the Graduate School of

The University of Texas at El Paso

in Partial Fulfillment

for the Degree of

MASTER OF ARTS

THE UNIVERSITY OF TEXAS AT EL PASO

August, 1983

Acknowledgements

I would like to thank the members of my thesis committee, Dr. Judith Goggin, Dr. James Devine, and Dr. William Reid. I want to give a very special thanks to my chairman, Dr. Donald Moss, for his unending patience, good humor, and commitment to this project. In addition, I am very grateful to Chris Chinnici for her help in the initial preparation of the radial arm maze, to Lisa Rodriguez for giving so freely of her time to assist in running the cholinesterase assays, and to Diane Herold for her role as intermediary between me and the word processor. I am especially indebted to Dr. Rick Steger who graciously ran the monoamine assays.

Abstract

This series of experiments was designed to determine if a centrally acting cholinesterase inhibitor could be used to facilitate memory in aged rats. Data were gathered in three areas: motor abilities, behavioral measures, and biochemical assays. The results replicated earlier studies that showed age-related decrements in performance on the tight rope, spontaneous alternation, and radial arm maze tests. The experiment failed, however, to overcome these deficits using a cholinesterase inhibitor. The most likely explanation appears to be that the level of CNS cholinesterase inhibition produced in these experiments was greater than was optimal for facilitating problem solving in rats. These experiments do demonstrate, however, that pharmacologically and behaviorally significant levels of CNS cholinesterase inhibition can be produced without the extreme toxicity associated with conventional cholinesterase inhibitors.

Table of Contents

	Page
Acknowledgements	iv
Abstract	v
List of Tables	vii
List of Figures	viii
Introduction	1
Methods and Results	16
Experiment 1	16
Experiment 2	22
Experiment 3	25
Experiment 4	34
Discussion	39
Appendix	45
Reference Notes	51
References	52
Vita	62

List of Tables

Table		Page
1	Tight Rope Behavioral Ratings.	18
2	Tight Rope Tests Mean Scores	21
3	Tight Rope Tests Analysis of Variance Results. . .	23
4	Spontaneous Alternation Tests 1-2 Pooled Data Results.	26
5	Spontaneous Alternation Tests Results.	27
6	Radial Arm Maze Analysis of Variance Results: Correct Responses.	33
7	Radial Arm Maze Analysis of Variance Results: Total Responses.	35
8	Cholinesterase Per Cent Inhibition	41

List of Figures

Figure		Page
1	Correct responses of the three age categories over 15 trials.	31
2	Correct responses of drug and control condition animals in each age category.	32
3	Cholinesterase activity in the cortex expressed as a percentage of the young control condition. .	40

The general purpose of this research was to use an animal model that parallels the decrements in cognitive abilities found in aged humans to ascertain if these deficits can be reduced or eliminated through facilitation of the cholinergic system. Specifically, the purpose of the research was to study the behavioral and biochemical effects of phenylmethylsulfonyl flouride on aged rats.

Alzheimer's Disease

Senile dementia, the steady deterioration of memory and other cognitive functions (Folstein, Folstein, & McHugh, 1975), afflicts an estimated 1.5 million Americans, or approximately 15% of the population over 65 years of age (McKinstry, 1982). In fact, 60-80% of nursing home patients are demented (Kolata, 1981). The most common form of dementia is senile dementia of the Alzheimer's type (SDAT), accounting for at least 50% of the dementia cases (Katzman, Terry, & Bick, 1978). The incidence of SDAT has been reported as early as 40 years of age (McKinstry, 1982), and the risk of SDAT increases with progressing age, especially after 65 (Appel, 1981). A government study (1977) predicts an increase in the percentage of the population over 65 from 9.9% in 1970 to 11.7% by 1990. As the proportion of elderly living past 65 increases, the number afflicted by SDAT will increase substantially and could potentially become one of the major health problems in this country (Appel, 1981).

The course of SDAT is characterized by an insidious onset, with loss of memory for recent events, a gradual, progressive degeneration of cognitive functions, neurological impairment, such as difficulty in walking, and unremitting deterioration until the patient becomes bedridden and dies in a state of profound dementia (McKinstry, 1982; Yamamura, 1981).

Age-related morphological changes, such as senile plaques and neurofibrillary tangles (McKinstry, 1982; Yamamura, 1981), are found in the brains of most elderly individuals (Enna & Strong, 1981). However, in SDAT victims, these changes are quantitatively greater, and the number found is correlated with the degree of dementia suffered by the patient (Kolata, 1981). Additionally, Fuld (1978) reports that there is a similarity in the symptoms of memory loss between SDAT patients and normal elderly, with the difference being that the SDAT memory loss is more severe. The facts suggest that these aberrations may occur as a part of the normal aging process (Enna & Strong, 1981; Reisine, Yamamura, Bird, Spokes, & Enna, 1978), but their occurrence is greatly accelerated and exaggerated in the SDAT patient.

Age-Related Decrements in Memory

Studies of age differences in human memory indicate that certain memory functions decline with age (Craik, 1977). In his review, Craik (1977) interpreted the

results of several experiments involving age decrements in terms of primary and secondary memory. Primary memory refers to memory for material that is still at the focus of conscious attention. Secondary memory is a more permanent memory system, utilized when the capacity of primary memory is exceeded or when information is held past immediate attention. Craik (1977) concluded that decrements with age are minimal in primary memory. These results are based mainly on forward memory span tests using digits, letters, or words (Drachman & Leavitt, 1972). Talland (1976) also concluded that, if rehearsal is allowed, recall from primary memory does not change with age. Similarly, Keevil-Rogers and Schnore (1969) found that digit recall was a function, not of age, but the length of the retention interval or the interval activity.

Age differences are most often observed, however, when the limits of primary memory are exceeded (Craik, 1977). In backward span experiments (Bromley, 1958), where the subject must repeat the items in reversed order, reliable decrements with age are observed. This type of task, where stored material must be manipulated or reorganized, led to disproportionate difficulty in the elderly (Broadbent & Gregory, 1965). Tests of learning of supraspan digits and cued and uncued free recall of words showed highly significant impairment in the elderly (Drachman & Leavitt, 1972).