THE DIETARY INTAKE OF LECITHIN, METHIONINE AND PROTEIN IN PATIENTS WITH ALZHEIMER'S DISEASE

A THESIS

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We hereby recommend that the Thesis prepared under our supervision by Stephanie Anne Wiorek entitled The Dietary Intake of Lecithin, Methionine, and Protein in Patients with Alzheimer's Disease

be accepted as fulfilling this part of the requirements for the Degree of Master of Science.

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Like a curtain of the stage is the best way I can describe this accomplishment in my life. Behind it lies many responsible for that which it exposes, never seen before. My greatest thanks are deserving of my God. It was He who gave me my wonderful family with their unsurmountable love and patience, and all my friends who have stood with me during some of the hardest times of my life. My gratitude goes out to so many, especially: J.S. Meyer, M.D., T. Shaw, Ph.D., S. Brinkman, Ph.D., M. Cutaia, M.A., K. Mortel, M.S. and the rCBF staff. Thanks for all your help and guidance. To Karen, thanks for putting up with the million and one calls, and Lea, for the second million. Thanks to C. Sajadi, M.D. for your input. Special thanks to Kathy Lawson and the rest of my thesis committee. Last but not least, I want to thank John and everyone who had faith in me and my study. I will never forget all your time and patience either, because there were some real rough moments.

As one author stated "friends are like flowers in the garden of life." God was truly generous when He gave me mine.

INTRODUCTION

More than 22 million people in this country or approximately 11% of the U.S. population are currently over age 65, with a projection of 16-20% by the year 2030 (Schechter, 1980; Department of Health, Education and Welfare, 1979). Over one million of these elderly individuals are institutionalized or cared for at home primarily because of reduced mentation, diminished cognitive functions and other forms of psychological dysfunction commonly termed dementia.

More specifically, Fischer (1968) defined dementia as a chronic reduction in higher verbal and non-verbal cerebral functioning. It is a progressive decline in cognitive abilities which can arise from a number of etiologies (Tomlinson, 1977). Symptoms of the disorder include poor memory, loss of familiar skills, impaired social judgment and lability of affect (Kaszniak et al, 1979).

Behavioral impairments attributable to age-related conditions affecting the brain are perhaps the most significant causes of loss of competence among the aged. Most symptoms of cerebral disorders are increasingly more frequent after age 65. In general, aging leads to a growing inability of the organism to adapt to the environment and thus to survive. The result is a decline in physiologic

competence in these people which decreases motor functioning and increases the incidence and intensity of accidents, disease, and other forms of environmental stress (Timiras, 1972).

One of the most perplexing conditions affecting the brain is Alzheimer's disease (AD), which may involve the selective loss of central cholinergic neurons throughout the brain. In approximately 40% of patients classified as demented, AD is present (Davies et al, 1976). Normally, there is a gradual but progressive loss of neurons associated with the aging process; however, neuronal atrophy is apparently accelerated in AD (Davies et al, 1976).

Brain autopsy and biopsy studies have demonstrated that patients with AD may have a specific loss of brain cells containing acetylcholine (ACh). Recently, this disease has been shown to be associated with a partial loss of neurons that synthesize and utilize ACh, as well as with a reduction in the activity of the brain enzymes that form ACh from choline (Kolaia, 1979). Several studies have revealed that choline acetyl transferase (CAT) activity is reduced in AD (Davies and Mahoney, 1976; White et al, 1977; Perry et al, 1977), suggesting that substances which increase ACh activity might help to improve cognitive functioning in patients with AD. These substances include choline, physostigmine, choline chloride, and lecithin (phosphatidylcholine).

The body does not manufacture choline in appreciable amounts (Wurtman, 1979). Since choline is necessary for the synthesis of ACh, the body must have a continuous dietary supply of choline. The primary source of dietary choline is lecithin and almost all of the choline that humans consume is in the form of lecithin. Major food sources include eggs, liver, cauliflower and kale. In addition, lecithin is commercially available and used widely in the food industry as an emulsifier. Raw or crude lecithin contains about 27% to 37% soybean oil, 2% moisture and impurities, and 60-70% phosphatides (Wurtman, 1979). Further refining of the lecithin removes most of the oil, leaving these substances in varying amounts. Commercial lecithins available to the consumer contain only 20-30% phosphatidylcholine.

Based upon the supposition that symptoms associated with AD may be directly related to deficient lecithin intake, several researchers have conducted trials with dietary supplements of lecithin or choline and found beneficial effects in cognitive functioning when lecithin was administered (Etienne et al, 1978). The suggestion from Etienne's pilot study was that oral doses of lecithin might be of benefit to AD patients at an early stage of progression. Another study indicated that supplemental lecithin given with physostigmine, a centrally active acetylcholinesterase inhibitor, appeared to allow this substance to augment

memory in AD, suggesting that a nutritional factor may influence this condition (Peters et al, 1979). Evidence of impairment in central cholinergic function and encouraging preliminary responses of patients with AD to dietary treatment warrants further investigations into the role of lecithin with AD (Davies et al, 1976).

Additionally, the implication is that a need exists to assess the current consumption of lecithin in the American diet (Wurtman, 1979). There has been no requirement set for this substance in the U.S. Recommended Daily Allowances (RDA's). Since choline may also be endogenously synthesized in small amounts from the essential amino acid methionine, it seems necessary to simultaneously assess dietary intakes of methionine and protein in addition to lecithin.

STATEMENT OF PROBLEM

The purpose of this study was to investigate the following question: Does a difference exist between the dietary intake of lecithin, methionine and protein in patients with early, putative Alzheimer's disease and a similar age-matched group?

DEFINITIONS

1. PUTATIVE - Generally thought of as such; supposed.

2. SENESCENCE - "Senility" Describes a large number of conditions with an equally large number of causes. The symptoms include forgetfulness, disorientation, intellectual confusion and certain other medical and emotional disturbances (U.S. Department of Health, Education and Welfare, 1979).

3. 24-HOUR FOOD RECALL - A compilation of all foods consumed during a "typical" 24-hour period. Included in the data are amounts and brand names for all meals and snacks eaten.

4. FOOD FREQUENCY LIST - A compilation of foods high in lecithin, methionine and protein to determine consumption patterns followed. Used to enhance data obtained from the 24-hour recall period used.

REVIEW OF LITERATURE

Lecithin, a phospholipid, consists of glycerophosphoric acid, and esters of oleic, stearic or other fatty acids combined with choline. Found in many tissues, lecithin is most widely distributed in the dendrites and axons of nerve cells. The biosynthesis of this phospholipid depends on a diet rich in sources which supply choline or methyl groups. It is an essential component of cell protoplasm. Where it is present as a dipolar ion with choline acting as a strong base, it has a major role in fat transportation to the tissues (Routh et al, 1969).

The endogenous synthesis of choline requires the presence of two amino acids, serine and methionine (Williams, 1974). Serine in addition, can be used to synthesize choline in vivo. Considering that the main function of choline is essentially methyl donation, its effectiveness in the body is dependent on the methyl groups in its structure. A deficiency of dietary protein and methionine, whose presence contribute to the synthesis of choline, thereby affecting its biosynthesis, may result in a deficiency of the necessary methyl groups (Briggs and Calloway, 1979, pp. 207; Harper et al, 1979).

Alterations in dietary choline intake can affect brain

functioning, as well as levels of acetylcholine (Harper et al, 1979). Acetylcholine (ACh) is a chemical mediator of the parasympathetic nervous system as well as having other activities in the CNS. There is evidence that alterations in the distribution and function of the neurotransmitters may have recognized manifestations, including several neurologic and psychiatric disorders (Omenn, 1976), and it has been suggested that alterations in dopamine and norepinephrine may occur during senescence (Lytle and Altar, 1979; Harris et al, 1979).

Attempts have been made to elevate levels of ACh by the administration of precursors such as choline and/or lecithin. Such therapeutic attempts seem to be justified in restoring noted deficiencies (Boyd et al, 1977; Etienne et al, 1978; Signoret, Whiteley and Lhermitte, 1978). However, should major losses of cholinergic neurons or their synaptic terminals exist, these same attempts may be destined for failure.

The enzyme, choline acetyl transferase (CAT), is found within the mammalian brain. It has been widely accepted that CAT is only found in the cholinergic neurons (Kuhar, 1976). CAT has been found to be 10 to 30% less in AD than levels found in age-matched normal subjects (Pope, Hess and Lwein, 1965; Brown et al, 1976; Davies and Mahoney, 1976; Perry et al, 1977; White et al, 1977; Reisine et al, 1978).

In a study of eight elderly patients with mild memory impairment, Mohs et al (1979) provided each subject with choline chloride. One conclusion made was that although animal studies have indicated that choline chloride may increase brain ACh concentrations, it does not necessarily follow that choline increases central cholinergic activity. Several researchers have made reference to ACh, indicating that there appears to be a decrease in its uptake with age, resulting in decreased levels of this neurotransmitter and alterations in CNS glial cells and neurons (Lytle and Altar, 1979).

Evidence exists indicating that in AD, major deficits are present primarily within the cholinergic system (Terry et al, 1980). Studies using cholinergic substances including physostigmine, choline, arecholine, acetylcholine and lecithin have been performed in an attempt to identify long and short-term changes in memory functioning. Overall, results have shown that supplementation with these substances may produce notable improvements in learning (Lehman, 1979; Hoffmeister and Müeller, 1979). Muramoto et al (1979) acknowledged the beneficial affect of physostigmine in the treatment of AD; however, it must be noted that the subjects under study were in the severely demented state.

Impaired brain cholinergic function has been proposed as a mechanism for memory and cognitive (M/C) disorders of

the aged (Drachman et al, 1979). This originated from the observation that the administration of scopolamine, a central cholinergic blocking agent, produced a pattern of M/C changes in young subjects closely resembling that commonly observed in the elderly. Further studies were performed using scopolamine with the elderly and the results were reproduced, supporting the hypothesis that the decline in M/C in AD may be the result of an impaired functioning of the cholinergic neurons (Drachman et al, 1979).

Mohs et al (1979), using a volunteer subject pool of healthy elderly individuals (7 women and 1 man) with mild to moderate memory impairment, screened for health problems with no significant illness observed. A placebo-drug-placebo schedule was used for a 35 day study period. Sixteen g/day of choline was administered from day 8-14, and a placebo was given on the other days. Those subjects with the poorest baseline performance showed greatest improvement in memory functioning.

All cells age, grow senescent and eventually die. Thus, there is no reason to suspect that CNS cells are immune to this process. Neurons within the CNS do not undergo mitosis and regenerate. They cease to divide early in life and are near maximum in number at birth. In addition, there has been shown to be a progressive decline in cell number within the brain, beginning at about the end of the growth and maturation period (Shaw, 1980).

Decline in memory and the ability to learn with increasing age are problems commonly observed in AD patients. The high susceptibility of the brain to nerve cell loss results in age-related changes in the CNS including the breakdown of the blood-brain barrier, restricting the exchange of water soluble drugs and proteins between the blood and brain. Such changes have been suggested by the Department of Health, Education and Welfare (1980) to be in need of further investigation.

The National Institute on Aging (NIA) places high research priority on the relationship between the CNS and nutrition (Butler, 1979). One investigation supported by this group observed neurotransmitter levels and enzymes in the brains of aged subjects. Levels of tyrosine hydroxylase, decarboxylase, dopamine and norepinephrine were found to be lower than normally found in young adults. To follow-up these findings, rodents were fed a diet high in lecithin, resulting in elevated choline and acetylcholine measurements in the brains and adrenal glands of these animals. The results suggest that acetylcholine may be under short-term nutritional control.

Other dietary manipulations using rodents have been performed. Levels of tyrosine, tryptophan or choline were manipulated in an attempt to evaluate changes in brain neurotransmitter levels. Diets limited in these nutrients

resulted in marked decreases in the synthesis of dopamine and norepinephrine, serotonin, or acetylcholine respectively (Lytle and Altar, 1979). This data suggests that diminished neurotransmitter uptakes may be related to aging when diets become nutritionally inadequate in vitamins, minerals and proteins.

These and other experimental studies with rodents have shown striking changes in brain and neurotransmitter function; hence, nutrition-induced changes in the CNS of the elderly may be more insidious and commonplace than once thought (Wurtman et al, 1977; Lytle and Altar, 1979).

The elderly constitute a segment of society prone to the side effects of nutritional inadequacy. The Recommended Daily Allowances (RDA's) are designed to meet the nutritional needs of the majority of the healthy population with a margin of safety. RDA's for the elderly, however, are merely generalizations from younger population figures, with the exception of calorie requirements (Schaefer and Korth, 1980). Decreases in metabolism, lean body mass and physiological activity warrant the need to decrease caloric intake as aging occurs. It has been speculated that caloric needs decrease as much as 16% for someone 65 from the amounts recommended at age 22 (Busse, 1978; Munro, 1978). In essence, this means that a more nutritious diet per calorie is required for the elderly (Schaefer and Korth, 1980).

All suspected CNS transmitter chemicals are nutrient components of the diet. Included in this group are protein, amino acids and lipids necessary for proper CNS functioning. Minor changes in the quantity or quality of intake have revealed changes in brain neurotransmitters, particularly acetylcholine, as well as several behavioral and physiological patterns (Lytle and Altar, 1979; Growdon, 1979).

It has not been demonstrated that man is subject to choline deficiency. However, inadequate levels of other dietary components such as protein and methionine may result in decreased choline synthesis. Concern exists with regard to this when the dietary intake of nutrients or their availability to the tissues becomes inadequate for extended periods of time. The end result from such occurrences may be altered enzyme activity inhibiting optimal utilization of phosphatidylcholine, reduced total proteins and metabolically active compound formation, and/or changes in the efficiency of dietary energy utilization (Lytle and Altar, 1979; Pike and Brown, 1975, pp. 175). Changes such as these are important factors in determining the cause of aging and its effects on various body systems.

Several investigators have shown that the protein intake of young and old persons vary only slightly (Stephen, 1973; Young and Scrimshaw, 1975, 1979). One study by Stiedman et al (1978) showed elderly men and women had daily intakes of

67.3g $\pm$ 3.2 and 48.0g $\pm$ 2.7, respectively. The mean level obtained for the total subject pool (aged 60-84) was found to be 57.7g $\pm$ 2.9. This figure compares favorably with the RDA (women: 44g; men: 56g). Brown et al (1977) observed the mean daily intake of protein to be 60.3g in a group of independent-living elderly, a value once again exceeding the RDA.

In an earlier study, Frey et al (1963) noted an intake of 66.1g protein/day, in a group of elderly female Bostonians, with the intake of the overall Boston population being 65.8g. Using the present standards for dietary adequacy, it would seem that there is no dearth of protein in the diet of these populations.

The need for methionine, an essential amino acid, is thought to increase with age. Some research (Guthrie, 1975) has indicated that amino acid requirements differ in young and old, but no definite amount has been determined due to population individuality. Briggs and Calloway (1979) determined the minimum daily requirement for methionine in the adult to be 910mg. Presently, only suggested levels of methionine exist, and although differences have been indicated with the aging process, the recommended intake of this amino acid varies among investigators.

Unfortunately, the only information available pertaining to lecithin intake comes from studies done during the

late 1940's and early 1950's (Hirsch and Wurtman, 1978; Best and Lucas, 1962). At that time the proliferation of processed foods, increased fast food chains, recommended decreases in egg consumption, and an increased consumption of food supplements had not yet begun. Intake from natural sources of lecithin was speculated to be 5 to 6g/day. However, after an evaluation of 3-week dietary recalls, J. Wurtman (1979) estimated lecithin consumption for the average adult today to be as low as .759g/day. Using a hypothetical situation in which an adult consumed large amounts of chocolate, it was observed that lecithin levels might increase to as much as 3g/day from the level previously indicated (less than 1g).

Lecithin, a natural constituent of almost all dietary sources has entered the food industry as an additive, an ingredient replacement and as a food supplement. Assuming commercial lecithins contain 25% phosphatidylcholine, a daily intake might be approximately 23mg. Wurtman (1979) believes that this figure is below the current consumption level, with increases in the previously noted proliferation of processed foods and lecithin addition to many foods. Recently, lecithin has joined the food supply as a constituent of torula yeast (a flavoring agent) with a concentration level of about 2.5-3%. There is difficulty in assessing the total intake of lecithin due to a lack of sufficient data on its content levels and the newness of torula yeast.

Several other nutrients have been studied with regard to their effects on brain functioning. Lehman (1979) used water soluble vitamins (especially vitamin C, B_{12} and nicotinic acid) and lipotropic enzymes (glucouronidase and cytochrome C) in the management of psychiatric disorders of the elderly. Patients treated with these substances showed marked improvement in their disabilities (Muramoto et al, 1979).

Finally, it has been suggested that brain DNA may gradually decrease due to a number of accumulated errors in replication (Blumenthal, 1978; Martin, 1979). This data has led to the belief that a flaw in protein synthesis may result in amino acid structure defects. Aluminum has also been speculated to interact with DNA causing a dramatic effect on the structure of its molecules, including clustered, enlarged or abnormal synaptic endings, altered axons and dendrites filled with degenerating cell organelles and increased concentrations of aluminum. Such changes have been noted in some regions of the brain in AD patients (Pfeiffer, 1975). Speculation has been made that such changes and lesions observed in AD result from a cross-link formation between aluminum and the DNA strands (U.S. Department of Health, Education and Welfare, 1979). Thus, what we are dealing with is a disease process that needs considerably more research in order to define its beginning, project a manner of treatment, and eventually, a means of prevention.

HYPOTHESIS

The hypothesis of this study is that the dietary intake of patients with Alzheimer's disease (AD) will be significantly lower in lecithin, methionine and protein than the diets of age-matched controls.

METHODS AND PROCEDURES

This project was conducted under the auspices of the regional Cerebral Blood Flow (rCBF) laboratory located at the Veteran's Administration Medical Center, Houston, Texas. J.S. Meyer, M.D. (Director) and T. Shaw, Ph.D., (Associate Director), of the rCBF lab supervised and assisted in the establishment of the sample populations. Diagnosis of Alzheimer's disease was based on complete neurological evaluation, EEG, CT-scan, neuropsychological assessment, and measurements of rCBF.

Two sample groups were formed consisting of putative AD subjects in an early stage of progression and age-matched, normal healthy controls. Each group was composed of 19 subjects, thus allowing for a total sample size of 38. All subjects were randomly selected from a larger population provided by the rCBF lab from an ongoing study of rCBF, aging and early dementia. These subject groups consisted of male and female subjects 45 years of age and older.

Each subject was admitted into this study on the basis of the following criteria:

1) Putative Alzheimer Group:

   a. Diagnosed by a neurologist as having relatively recent onset of Alzheimer-type symptoms.

b. Impaired memory function as measured by a standard neuropsychological assessment battery, EEG, CT-scan, neurological evaluation, and measurements of rCBF.

2) Age-matched Control Group:

a. These subjects received the same evaluation as the AD group, including neurologic and neuropsychological exam, EEG, CT-scan, and measurements of rCBF, with a resultant diagnosis as a healthy (non-AD) subject.

Each subject was supplied with a "typical" 24-hour dietary recall form on which he or she listed food items eaten, including amounts and brand names. The basis for using a 24-hour recall was established by Snowman (1979), in which the investigator reported no significant difference between one and three-day dietary recalls. In addition, to augment the 24-hour recall, all subjects were given a frequency list of foods known to be high in lecithin, methionine and proteins. These were obtained from the 13th Edition of Bowe's and Church's Food Values of Portions Commonly Used (1980) and Nutrition and the Brain (1979).

Each 24-hour recall and food frequency list for subjects in the putative Alzheimer's group was completed by a reliable family member. Assistance was given by family member(s) in order to minimize the possibility of incorrect and/or

incomplete dietary information, as one of the hallmarks of Alzheimer's disease is memory loss. The control subjects provided their own responses.

The independent variable in the study was group membership with two levels (age-matched normal controls and putative Alzheimer's). The three dependent variables were the levels of lecithin, methionine and protein.

Data analyses were conducted with the computer terminal located at the rCBF laboratory, Veteran's Administration Medical Center, Houston, Texas. The terminal used was an Infoton 400, linked to the Baylor College of Medicine Computer Center, Houston, Texas. This computer system allowed for the use of SPSS (Statistical Package for the Social Sciences) programs. The student t-test was used for the statistical analysis of all data except evaluation of the food frequency list, which was performed using the non-parametric test of significance chi-square.

RESULTS AND DISCUSSION

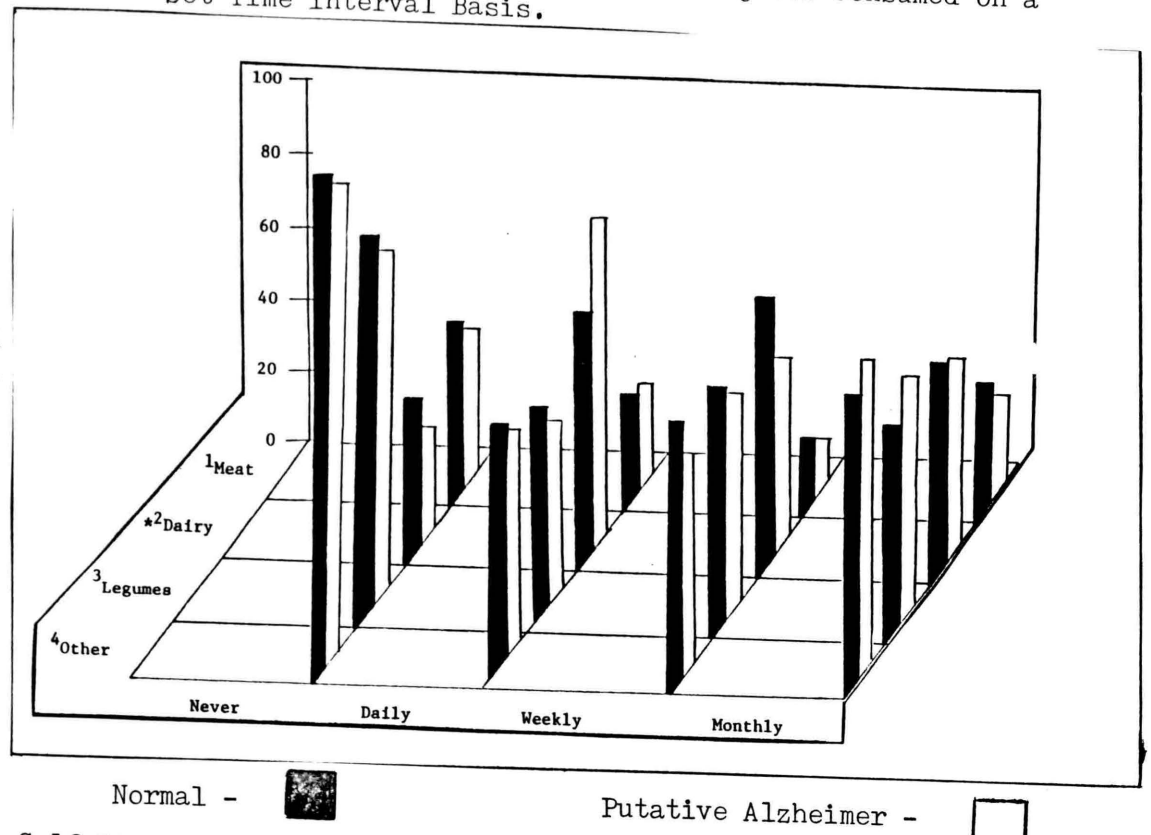
Analyses of lecithin, methionine and protein intake were performed in order to assess possible differences within and between the control and putative Alzheimer disease (AD) groups under study. The total number of subjects was 38, with 9 females and 10 males in the control group and 8 females and 11 males in the AD group.

This data was based on the assessment of "typical" 24-hour food recalls, and food frequency lists. The "typical" 24-hour recall form (See Appendix A) recorded brand names, amounts consumed and method of preparation. The forms were filled out with the assistance of family members who provided more detailed information than the AD members were able to provide, since memory loss is one of the hallmark symptoms of AD.

In addition, each subject/family member was personally contacted by the investigator and questioned as to the frequency of dietary intakes of various foods high in lecithin, methionine and protein. Quantity of food ingested was not recorded on this "food frequency" record (See Appendix B and Figure 1).

As seen in Figure 2, the mean intake of lecithin for the AD subjects, as determined by the "typical" food recall,

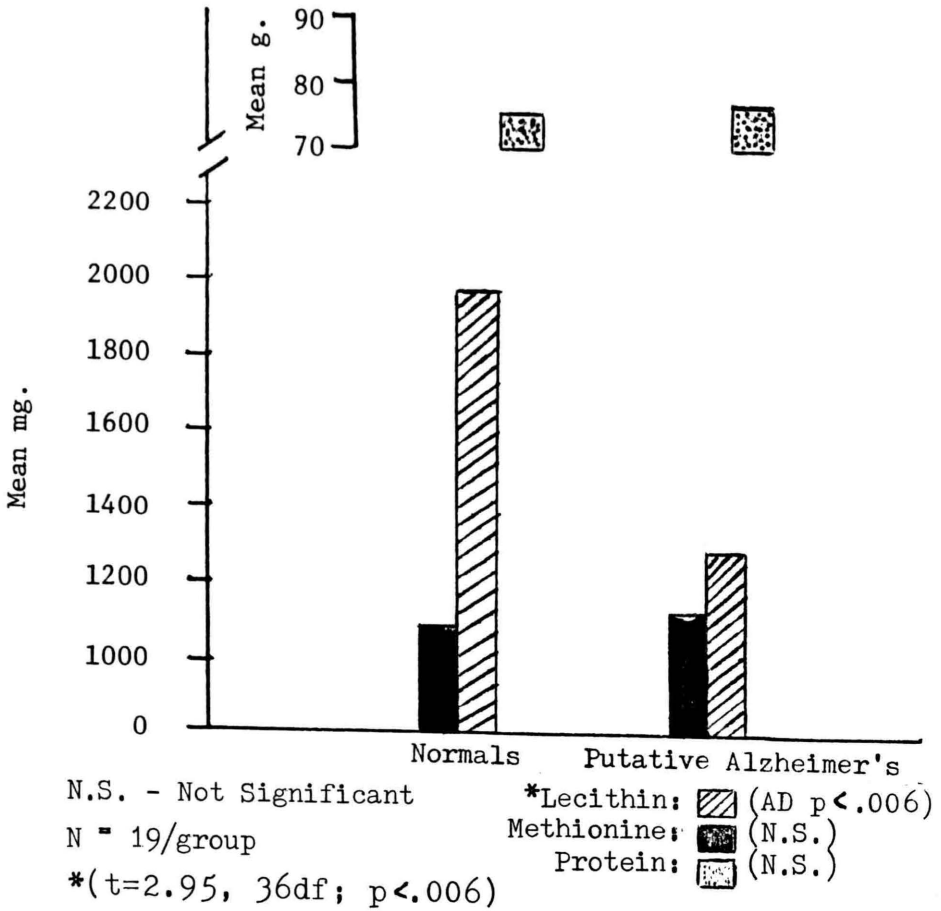
Figure 1: Comparison of High Lecithin, Methionine and Protein Foods in Normal and Putative Alzheimer Subjects Consumed on a Set Time Interval Basis.



1. Calf Liver, Fish, Lamb Chops, Meat (General-Beef), Poultry, Veal.
2. Cheese, Eggs, Milk.
3. Beans- Dry, Peanuts, Peanut Butter, Soybeans, Wheat Bran, Wheat Germ.
4. Asparagus, Brewer's Yeast.

*2 (χ^2 7.98, 3df; $p < .05$: Duration Intervals Not Inclusive With Comparison).

Figure 2: Mean Intake of Lecithin, Methionine and Protein in Normal and Putative Alzheimer Subjects From Assessment of "Typical" 24-Hour Dietary Recalls.



was significantly less than the control group ($t=2.95$, 36df; $p < .006$). No significant differences were observed in the other dietary components evaluated. According to the food frequency list (See Figure 1 and Table 1), dairy products, which have been noted to be high in lecithin, were consumed in significantly greater quantities by the AD group ($\chi^2=7.98$, 3df; $p < .05$). This difference is of interest in that it apparently indicates that even though there was a more frequent ingestion of these quality sources of lecithin by the AD group, the total amount consumed was actually less than that consumed by the normal controls. Apparently, although AD subjects consumed greater amounts of dairy products (on a weekly basis), their intake of other foods was decreased and thus the total amount of lecithin consumed must be realized as being from all foods eaten.

When the intake of lecithin between males and females was analyzed with no regard to diagnosis, females in both AD and normal control groups consumed slightly more lecithin and methionine in comparison to their male counterparts although the difference was not significant (See Tables 2 and 3).

All female subjects in the putative AD and control groups showed significantly greater intakes of lecithin, methionine and protein when compared to the RDA for women over age 65. On the other hand, males within both of these

Table 1: Intake of Foods High in Lecithin, Methionine and Protein Between Normal and Putative Alzheimer's Subjects on a Set Time Interval Basis.

NORMALS

	NEVER	DAILY	WEEKLY	MTHLY
MEAT	* 32	15	30	23
DAIRY	12	39	44	5
LEGUMES	58	11	18	13
OTHER	68	6	8	18

N = 19

PUTATIVE ALZHEIMER'S

	NEVER	DAILY	WEEKLY	MTHLY
MEAT	* 31	17	31	21
DAIRY	4	63	28	5
LEGUMES	53	7	17	23
OTHER	66	5	0	29

N = 19

* % of total subject population.

Table 2: Comparison of Recommended Daily Intakes of Lecithin, Methionine and Protein.

		NORMALS					PUTATIVE ALZHEIMER'S				
		N	MEAN INTAKE	t	df	p<	N	MEAN INTAKE	t	df	p≤
MALES	LECITHIN (RDA=700mg.)	10	1747.10 ±798.73	3.93	9	0.005	11	1367.37 ±605.13	3.49	10	0.005
	METHIONINE (RDA=910mg.)	10	921.82 ±381.66	N.S.	N.S.	N.S.	11	1095.49 ±665.68	N.S.	N.S.	N.S.
	PROTEIN (RDA= 56g.)	10	79.84 ± 24.66	2.90	9	0.010	11	86.68 ±29.73	3.26	10	0.005
FEMALES	LECITHIN (RDA=700mg.)	9	2235.51 ±906.69	4.79	8	0.005	8	1111.52 ±644.25	1.69	7	*0.100
	METHIONINE (RDA=910mg.)	9	1211.25 ±367.96	2.32	8	0.025	8	1180.78 ±809.49	N.S.	N.S.	N.S.
	PROTEIN (RDA= 44g.)	9	71.10 ±15.78	4.86	8	0.005	8	65.20 ± 30.80	1.82	7	*0.010

AGE:
Normals: Males - 61.9 ± 6.9 yrs. Putative AD: Males - 64.5 ± 10.2 yrs.
Females - 63.0 ± 7.1 yrs. Females - 64.6 ± 7.5 yrs.

*Computation Assuming Normal Distribution Potentially Inaccurate Due to Small N.

Table 3: Comparison of Recommended Daily Intakes and Reported Daily Intakes Between Sexes.

	MALES All Subjects					FEMALES All Subjects				
	N	MEAN INTAKE	t	df	p<	N	MEAN INTAKE	t	df	p <
LECITHIN *(RDA = 700mg.)	21	1548.20 ±712.70	5.32	20	0.0005	17	1706.58 ±962.83	4.68	20	0.0005
METHIONINE *(RDA = 910mg.)	21	1012.79 ±617.83	N.S.	N.S.	N.S.	17	1196.91 ±595.51	2.15	20	0.0250
PROTEIN *(RDA = (M) 56g. (F) 44g.)	21	83.42 ± 26.97	4.55	20	0.0005	17	68.32 ± 23.42	4.64	20	0.0005

* References

Barbeau, A., Growdon, J.H., and Wurtman, R.J. Nutrition and the Brain. Vol. 5 Choline and Lecithin in Brain Disorders. New York: Raven Press, 1979.

Briggs, G.M., and Calloway, D.H.: Bogert's Nutrition and Physical Fitness. 10th ed. Philadelphia: W.B. Saunders, Co., 1979.

Food & Nutrition Board: Recommended Dietary Allowances. 9th rev. ed. Washington, D.C.: National Academy of Science, 1980.

groups showed significantly greater intakes of lecithin and protein, but not methionine, when compared to the RDA's (See Table 3).

There were no significant differences in lecithin, methionine or protein intake between the sexes in either study group. This suggests that the results obtained could be generalized to both male and female subjects independently, and the study would have produced similar results if only one sex had been used.

The protein intake in all subjects was noted to be greater than the RDA's in most instances, while males revealed a slight, but insignificant, elevation of this nutrient when compared to females in both groups. There was no significant difference between AD and normal subjects with regard to protein intake.

No significant difference was found for methionine in either normal or putative AD subjects (See Table 4). The reported methionine levels in all subjects exceeded the "recommended daily intake" suggested by Briggs and Calloway used in this study. However, since no RDA has been generally agreed on, future recommendations may reveal changes in this evaluation.

Diets vary with age, and although the diets obtained in this study were typical of the subject's recent habits, they may vary from what the subjects consumed at a younger

Table 4: Comparison of Normal and Putative Alzheimer Subjects with Average Daily Intakes of Lecithin, Methionine and Protein.

		NORMALS				PUTATIVE ALZHEIMER'S			
	AVERAGE RDA	MEAN INTAKE	t	df	p <	MEAN INTAKE	t	df	p <
LECITHIN *(RDA = 700mg.)	700	1978.46	6.45	18	0.0005	1259.65	3.95	18	0.0005
METHIONINE *(RDA = 910mg.)	910	1058.92	N.S.	N.S.	N.S.	1131.40	N.S.	N.S.	N.S.
PROTEIN *(RDA=(M) 56g.) (F) 44g.)	50	75.70	5.38	18	0.0005	77.64	3.85	18	0.0005

* References

Barbeau, A., Growdon, J.H., and Wurtman, R.J. Nutrition and the Brain. Vol. 5 Choline and Lecithin in Brain Disorders. New York: Raven Press, 1979.

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age. Thus, in an attempt to augment the "typical" 24-hour recalls, the food frequency list was designed. The intent of this questionnaire was to identify which food sources were chosen most by the two groups throughout their lives.

The supplementation of lecithin to the diets of AD patients formed the basis of this study. Its deficit in the diet throughout life or during the later years still remains a mystery in determining at what point decreased levels have their greatest effect on the CNS. The unsolved mystery is very similar to when the occurrence of impaired cholinergic functioning actually begins.

As previously stated by Lytle and Altar (1979), diminished neurotransmitter uptakes may be related to aging when diets tend to be nutritionally inadequate in vitamins, minerals and protein. Thus, normal brain functioning may be affected at this time since all CNS transmitter chemicals are nutrient components of the diet.

Although methionine and protein levels were at or above the recommended amounts set in the study, this does not mean that there are no dietary implications when dealing with AD. It does, however, suggest that there may be other dietary factors involved that were not investigated at this time. In addition to methionine and protein, vitamins B_{12} and folic acid are involved in methyl synthesis and transfer in choline synthesis (Harper et al, 1979). Their involvement

in AD would seem to be warranted when looking further into a nutritional involvement with AD.

In spite of some seemingly significant results in terms of dietary intake, disease state and gender, the most significant source of error in this study is felt to be the fact that there is a lack of sufficient information provided by the manufacturers as to the lecithin content of foods. On the whole, the companies were not able to provide the necessary data on lecithin content. Responses noted certain components of the product to contain lecithin; however, the amount was not available. Several companies, who presently have no idea as to the level of lecithin in their products, did indicate a willingness to have the products evaluated for lecithin content.

In conclusion, it would seem justifiable to recommend further research considering such factors as other nutrient involvement, changes occurring in dietary intakes with age and the increased variances observed in disease states, in order to determine their involvement with AD.

SUMMARY, CONCLUSIONS AND IMPLICATIONS FOR FURTHER RESEARCH

Several authors (Barbeau, Groden, and Wurtman, 1979) have indicated that there is some possible disruption of the cholinergic system which seems to be related to Alzheimer's disease (AD). Barbeau (1978) pointed out that the action of dietary lecithin on this system remains to be clarified and that further investigation is warranted. It has been suggested that oral doses of lecithin, a major dietary source of choline, may be a way to keep patients at an early stage of Alzheimer's disease.

The intent of this study was to measure levels of lecithin, methionine and protein in putative Alzheimer disease subjects as opposed to normal, healthy controls. There was no difference in the intake of methionine and protein between the two study groups, nor between males and females in either group. However, the intake of lecithin was found to be significantly greater in the control group. Differences observed may in part be due to the fact that no specific levels for lecithin have been determined for most food items, resulting in difficulty in diet analysis. It was suggested by J. Wurtman that an analysis of lecithin consumption among various sub-groups in the population needs to be performed to provide information on base levels of lecithin

consumption.

The results of this study indicate that the normal, healthy subjects did indeed differ from the putative Alzheimer subjects in lecithin consumption. Further, in looking at the consumption of foods high in lecithin content, normal subjects consumed less dairy products (which are good sources of lecithin) on a daily basis.

While the literature points out that oral intake of lecithin might indeed be a deterrent towards the early onset of Alzheimer's disease, dietary consumption of lecithin has never actually been evaluated (Wurtman, 1979). For example, when the present data was evaluated against an average intake of lecithin obtained from the work of Wurtman (1979), there was a significant difference between levels observed in putative AD as opposed to normal, healthy subjects.

Considering the results, it seems suggestive that daily oral intakes of lecithin-containing foods in the diet needs further evaluation. To facilitate a more accurate evaluation of this data, it may be feasible to look at the dietary consumption of foods both low and high in lecithin content in both normal and early AD subjects. Given the fact that the study was a cross-sectional design, a further recommendation would be to evaluate foods high in lecithin using a more longitudinal design (within subjects repeated measures).

With the wide use of lecithin as an emulsifying agent

in the food industry, it is further suggested that more complete data be made available on the lecithin content of food products. Until such lists are defined, definitive results when evaluating diets for this constituent would be impossible.

APPENDIX A

DIETARY RECALL FORM

Name _____ Date _____ Day _____

FOOD	ESTIMATED MEASURE	INGREDIENTS/BRAND
BREAKFAST		
SNACK		
LUNCH		
SNACK		
SUPPER		
SNACK		

APPENDIX B

FOOD FREQUENCY LIST

PLEASE INDICATE HOW OFTEN THESE FOODS HAVE BEEN EATEN AS PART OF THE DAILY DIET. USE THE FOLLOWING CODING:

M	MAYBE ONCE A MONTH
N	NEVER
W	WEEKLY
D	DAILY
O	OTHER

____ ASPARAGUS	____ MILK
____ BEANS, DRY	____ PEANUTS
____ BREWER'S YEAST	____ PEANUT BUTTER
____ CALF LIVER	____ POULTRY
____ CHEESE	____ SOYBEANS
____ EGGS	____ VEAL
____ FISH	____ WHEAT BRAN
____ LAMB CHOP	____ WHEAT GERM
____ MEAT (GENERAL)	

IF YOU DID NOT INDICATE NEVER OR DAILY, PLEASE GIVE EXPLANATION: _____

_____

_____

_____

_____

_____

_____

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