Performance on Cognitive Skills Abilities by Age and Family History of Dementia

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Introduction

Dementia is a general term for the loss of memory and other intellectual abilities serious enough to interfere with daily life (http://www.alz.org/, 2007). Approximately 25%-45% of persons over the age of 85 years have Dementia. Alzheimer's disease (AD) is the most common form of age-related dementia and one of the most serious problems in the U.S. with an estimate of four affected individuals. Alzheimer disease (AD) is characterized by dementia that typically begins with subtle and poorly recognized failure of memory and slowly becomes more severe and, eventually, incapacitating (Bird, 2007). About 25% of all AD familial (i.e., two or more persons in a family have AD) of which about 95% is late-onset (after age 60-65 years) and 5% is early-onset (before age 65 years) (Bird, 2007). Additionally, multiple studies have shown that the prevalence of AD increases with age.

Alzheimer's Disease (AD) is a progressive and insidious neurodegenerative disorder of the central nervous system characterized by global deficits in cognition ranging from loss of memory to impaired judgment and reasoning. (Tanzi and Bertram, 2001) Further research has indicated that there is a genetic linkage to the onset of Familial Alzheimer's Disease (FAD). The Apolipoprotein Epsilon (APOE) 4-allele has been well-known to be the major biomarker in the genetic predisposition to Dementia. Initial estimates suggested that individuals with one copy of APOE4 had a three-fold risk of AD, while APOE4 homozygous has an eight-fold risk relative to non-APOE4 genotypes (Corder et al., 1993). Recent data suggest that APOE4 may be associated with increased rates of memory loss and decreased learning ability, while the converse may

apply to APOE2. In addition, these data are consistent with the findings that APOE genotype correlates with the functional activities of daily living in non-demented elderly individuals (Soininen and Riekkinen, 1996). These data are consistent with the findings that APOE4 genotype correlates with the functional activities of daily living in non-demented elderly individuals.

Research Question 1: Will a family history of Dementia predispose individuals to lower performance in cognitive skills tests than those with such family history?

The focus of this study is to examine the difference in cognitive performance for those who have relatives with Dementia compared to those who do not. It is expected that over the three time points, 1991, 1998, and 2005, subjects who have relatives with Dementia will have low levels and/or slopes for six dimensions of cognitive abilities. These dimensions include Verbal Memory, Numeric Facility, Inductive Reasoning, Spatial Orientation, Perceptual Speed, and Verbal Ability (Schaie, 2005). Three distinct age groups and sex was taken into account to highlight the decline in cognitive skills performance over three occasions.

Research Question 2: Are individuals with the Apolipoprotein Epsilon (APOE) 4-allele at a higher risk of developing Dementia due to a family history of this neurodegenerative disease?

Past research have pin pointed a genetic link between the development of Dementia and family history. However, there has not been profound analysis of the effect of the APOE 4-allele and a higher risk of inheriting the gene. Blood samples have been collected from participants from 1956 till 1998 to determine which APOE allele was predisposed individuals to this

neurodegenerative disease (Schaie, 2005). This data was then merged with the dataset of those individuals with a family history of Dementia. It is expected that those with the 4-allele will be at high risk of becoming stricken with Dementia specifically if they have a family history.

Methods

Performance on Cognitive Skills Test

Participants: A sub-set of participants through the Seattle Longitudinal Study was included in this study (N=1482); (Males=660 and Females=822). Sub-samples by age were also examined (Ages: N=22-42 years, N=43-63 years and N=64+ years). The Life Complexity Inventory (LCI) form was a survey administered to participants in the Seattle Longitudinal Study and "was designed to measure various aspects of our participants' immediate environment" (Schaie, 2005). These individuals reported any family history of Dementia, and whether they were dead or alive.

Design: Six dimensions of Cognitive skills were considered. They include Verbal Memory, Numeric Facility, Inductive Reasoning, Spatial Orientation, Perceptual Speed, and Verbal Ability. The abilities were examined at the factor level where the factor scores were computed from 3 or 4 marker variables for each of the abilities. Memory, Speed, and Reasoning decline are thought to be the best proxies for the progress of Dementia. The use of MANOVA helped link the relationship of whether those who have relatives with Dementia (RD) perform at lower levels than those who do not have relatives with Dementia (NRD). The performance of participants on Verbal Memory, Inductive Reasoning, and Perceptual Speed was hypothesized to show a decline from 1991 to 2005. Numeric Facility and Spatial Orientation were expected to have no relation to Dementia status, and Verbal Ability was expected to have no effect.

Analysis: Cross tabulations were done to determine optimal age grouping for use in a MANOVA design. The design of the MANOVA was 2 (RD vs. NRD) x 3 (Age-groups) x 2 (Sex) x 3 (Occasions) x 6 (Dimensions). The separation of age groups was necessary to evaluate whether subject's cognitive skills changed over the three occasions (1991, 1998, and 2005) to support the hypothesis. Mean tables were constructed to evaluate the significance amongst the variables (Sex, Age-group, Dementia, Dimensions, and Occasions). Main effects and interactions were examined to identify effects of performance level on the six dimensions for those in the RD group compared to those in the NRD grouping over the three occasions. The variables examined were Dimensions, Dementia, and Occasions. A second three-way interaction examined the distinction between the RD and NRD grouping for males compared to females over the three occasions. Here the variables examined included Dementia, Sex, and Occasion.

APOE 4-Allele

Participants: In the APOE 4-allele analysis, there were a total of 804 participants. These individuals originated from a sample size found in the Seattle Longitudinal Study by merging data from the original sub-sample group with _____. The mean average age of men and women were _____, respectively.

Design: The Statistical Analysis Software (SAS) was utilized in order to construct connection between individuals with or without APOE 4-allele to those with or without family

history of Dementia. In order to determine the APOE genotype of participants, blood samples were collected from the time period of 1956-1998 (Schaie, 2005).

Analysis: A 2x2 chi-squared analysis was performed for APOE (presence of 4-allele vs. without 4-allele) and family history of dementia (with family history vs. without family history). There were three allele categories: ALLELE, ALLELE1, and ALLELE2. However, the chi-square analysis indicated that ALLELE1 was the only significant data created with the comparison groups being those with any combination of the 4-allele to those without the allele. Within the ALLELE1 category, those in the allele1=1 contained 21.6% participants with demented relatives. However, those in the allele1=0 group had only 15% relatives.

Results

Performance on Cognitive Skills Test

Of the 1482 participants, 271 had relatives with Dementia and 1211 did not report relatives with Dementia. Subjects aged 22-42 had 23.68% relatives with Dementia compared to those 43-64 with 41.84% and of those who were 64+ with 34.48% having relatives with Dementia. Males within the RD group had an overall decline of 3.88 compared to females with a decline of 2.4 points. As expected, the males who have relatives with Dementia had a greater decline in cognitive abilities tests than those who do not have relatives with Dementia. While there was no overall significant difference between RD and NRD group, we found a number of statistically significant interactions. Examining these interactions, we found that there was a higher level of performance for NRD group on Verbal Memory, Inductive Reasoning, and

Spatial Orientation. In addition, on Perceptual Speed, the RD group had a steeper slope (decline) than did the NRD group. (Refer to Table 1 & 2)

	Male			Female		
	1991	**1998**	**2005**	**1991**	**1998**	**2005**
Relatives with Dementia	51.92	50.16	48.04	52.64	51.84	50.24
Relatives without Dementia	52.13	51.05	49.06	52.52	51.83	49.68

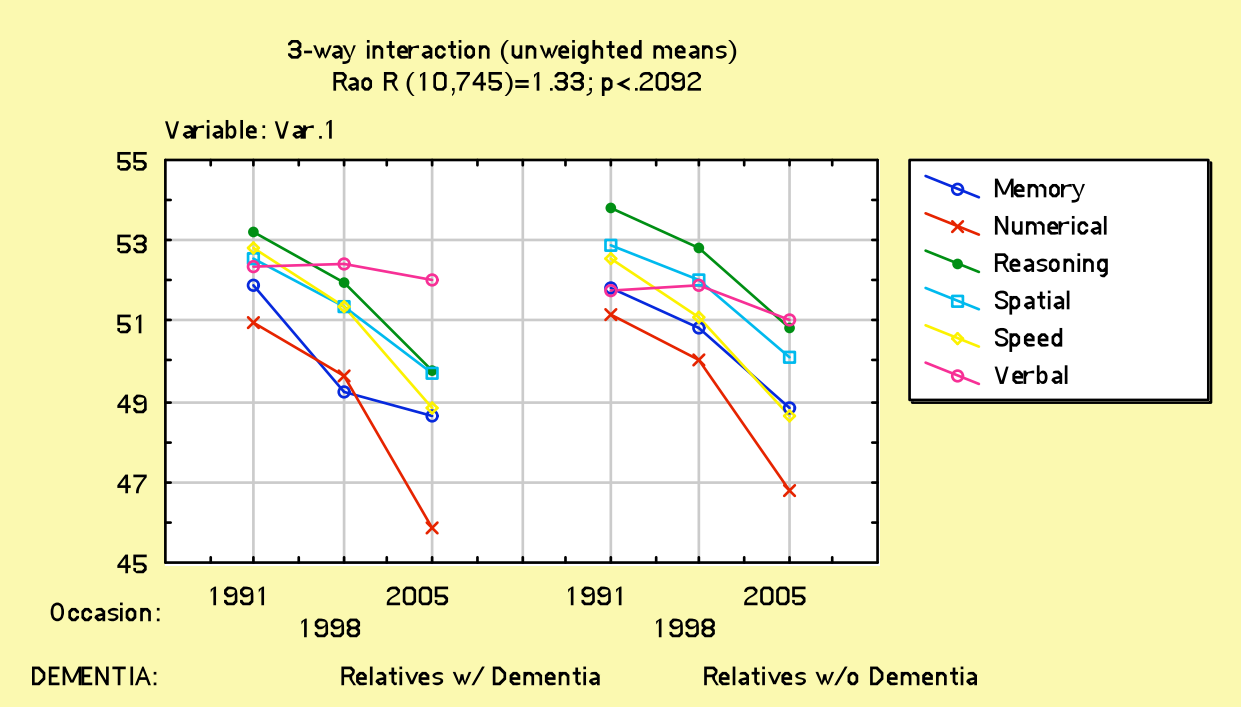
Table 1: This data suggests that at all time points, the means for males with demented relatives that performed at lower standards on the cognitive skills tests.

	T_1: 1991	**T_2: 1998**	**T_3: 2005**
Relatives with Dementia	52.28	50.00	49.14
Relatives without Dementia	52.33	51.45	49.38

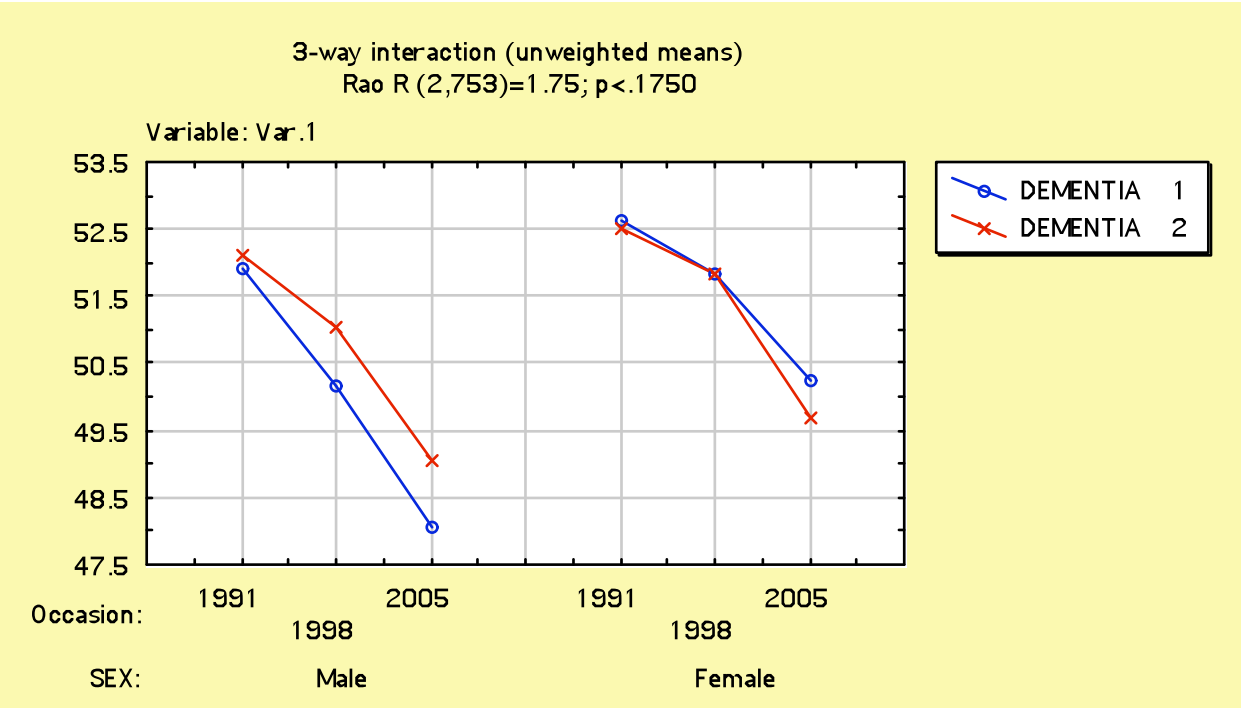
Table 2: The table illustrates the means for the total number of participants over the three time points for relatives with or without Dementia.

	Relatives with Dementia (DR)			**Relatives without Dementia (NDR)**		
	1991	**1998**	**2005**	**1991**	**1998**	**2005**
Memory Ability	51.89	49.27	48.64	52.80	50.82	48.84
Numerical Ability	50.96	49.65	45.87	51.18	50.00	46.76
Reasoning Ability	53.20	51.94	49.80	53.83	52.83	50.80
Spatial Orientation	52.54	51.34	49.72	52.86	52.03	50.10
Speed Perception	52.78	51.39	48.12	50.50	51.10	48.67
Verbal Reasoning	52.33	52.40	52.00	51.74	51.87	51.06

Table 3: This table depicts the mean scores for the six dimensions of cognitive skills assessment over the three time points for subjects who have or do not have relatives with Dementia.



Graph 1: The graph illustrates Dementia for the six variables over the three time points



Graph 2: This graph shows Sex and Dementia over the three time points.

APOE 4-Allele

A chi-squared analysis for APOE 4-allele and family history of dementia indicated a total of 804 participants. The mean average age of men and women were _____, respectively. The data was generated using SAS analysis program. There were three allele categories: ALLELE, ALLELE1, and ALLELE2. However, the chi-square analysis indicated that ALLELE1 was the only significant data created with the comparison groups being those with any combination of the 4-allele to those without the allele. In the ALLELE1 category, those with a 4-allele (coded as allele1=1) were compared to those without a 4-allele (coded as allele1=0). Those in the allele1=1 contained 21.6% participants with demented relatives. However, those in the allele1=0 group had only 15% relatives.

The 2x2 chi-square was performed for comparison purposes for the APOE 4-allele to participants with or without family history of Dementia. Results indicated ALLELE with no statistical significance (p=0.266), ALLELE1 was statistically significant (p=0.027), and ALLELE2 was not statistically significant but close (p=0.081).

	1	2	
0	Frequency: 88 Expected: 98.396 Cell chi-square: 1.0983 Percent: 10.95	Frequency: 498 Expected: 487.6 Cell chi-square: 0.2216 Percent: 61.94	586
1	Frequency: 47 Expected: 36.604 Cell chi-square: 2.9523 Percent: 5.85	Frequency: 171 Expected: 181.4 Cell chi-square: 0.5958 Percent: 21.27	218
	135	669	

Table 3: ALLELE1 = 0 (22,23,33); ALLELE1 = 1 (24,34,44); Family history of Dementia = 1; No family history of Dementia = 2

p>0.027; Chi-square value: 4.86

Discussion

Performance on Cognitive Performance Skills

The purpose of this study was to determine the difference in cognitive performance for subjects who have relatives with Dementia compared to those who do not. As time progressed, there was a slow decline in performance on the cognitive abilities tests. Age also played a role in determining one's capabilities to recall verbal information at a normal speed, as well as reason. Individuals in the 43-63 age group had a larger proportion of relatives with Dementia. However, the role of familial Dementia is ability-specific and most noteworthy for Verbal Memory and Reasoning abilities. Such data are important because data found that the elderly population would increase from 35.3 to 39.0 in 2030 (He, Sengupta, Velkoff & DeBarros, 2005).

APOE 4-Allele

Based on this data, participants with family history of Dementia and possess any combination of the APOE 4-allele have a higher than expected observed versus expected value. The cell chi-square value also validates those participants with the APOE 4-allele and demented relatives are at a higher risk of cognitive decline. Row 2, column 1 is the major contributor to the significance of the findings because of its higher than expected cell chi-square value compared to the other groupings. In total, individuals with any combination of the 4-allele had a higher frequency of reporting family history of dementia compared to those who had no family history or who did not have the 4-allele.

Conclusion

In general, these participants have been taken from a Health Management Organization (HMO) group in an urban Seattle, Washington area. Their education level has been known to be

higher than the average American populace. Their reporting of job placement indicates the education level achieved. At the same time, those in a lower SES grouping have been under-estimated. The racial demographics may not have played an intrinsic role in the outcome of performance level due to Familial Dementia but there was still an over-representation of Latinos and Asian-Americans. Because of Washington's close proximity to California, there has been a great migratory influence on the sample population. In addition, these individuals move to seek a better living a higher level of education for themselves and future generations. Therefore, it is possible that these individuals fare better on cognitive skills tests than other ethnic groups.

Developing research to determine whether a family history plays an integral role in cognitive development is crucial. Early detection is imperative in order to identify risks of the disease at an early stage so innovative pharmaceutical research and cognitive skills training may slow the development of the disease process.

References:

Alzheimer's Association (2007). *What is Alzheimer's?* Retrieved October 9 2007 from http://www.alz.org/alzheimers_disease_what_is_alzheimers.asp.

Bird, T.D. (2007). Alzheimer's Disease Overview. National Human Genome Research, NIH. Retrieved October 28 2007 from http://www.geneclinics.org/profiles/alzheimer/details.html.

Corder E.H., Saunders A.M., Strittmatter W.J., Schmechel D.E., Gaskell P.C., Small G.W., et. al. (1993). Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science, 261*(5123), 921-3.

He, W., Sengupta, M., Velkoff, V.A., & DeBarros.K. (2005). *65+ in the United States: 2005*,

U.S. Census Bureau, Current Population Reports. Washington D.C.: U.S. Government Printing Office.

Rubinsztein, D. (1997). The Genetics of Alzheimer's Disease. *Progress in Neuronbiology*, *52,* 1447-454.

Schaie, K.W. (2005) *Developmental Influences on Adult Intelligence: The Seattle Longitudinal Study.* New York: Oxford University Press.

Soininen, H.S. & Riekkinen, P.J. Sr. (1996). Apolipoprotein E, memory and Alzheimer's disease. *Trends in Neurosciences, 19* (6), 224-228.

Tanzi, R.E., & Bertram, L. (2001). New Frontier in Alzheimer's Disease Genetics. *Neuron, 32,* 181-184.