Early Psychometric Indicators of Possible Dementia in Later Life: Apo E Genotypes and Cognitive Performance Among Middle-Aged and Older Community-Dwelling Individuals.

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Abstract

234 middle-aged (M = 47) and 267 older (M = 65) participants were tested for ApoE genotype, revealing similar distributions of allele-type pairings in both age groups. Scores on the Test of Primary Mental Abilities (PMA; Thurstone & Thurstone, 1949), from these participants were available from the 1984, 1991, and 1998 testing waves of the Seattle Longitudinal Study. Repeated-measures analyses of covariance were applied to determine the extent to which allele types were related to cognitive decline within the 2 age groups. On the inductive reasoning subtest, there were significant ($p < .05$) interactions among age group, allele type and occasion, and between allele type and occasion. Differential performance patterns related to allele types were then interpreted with respect to their possible utility in the pre-clinical assessment of the likelihood of later dementia.

Introduction

- The apolipoprotein E (Apo E) epsilon 4 allele has been found to be related to the incidence of Alzheimer's Disease (AD).
- Individuals with one Apo E epsilon 4 allele are more likely than those without any to be afflicted by AD.
- Individuals with two Apo E epsilon 4 alleles are much more likely than others to get AD.
- Possession of Apo E epsilon 4 alleles does NOT adequately predict the likelihood of AD among the normal population — individuals with 2 epsilon 4 alleles may never develop symptoms, while conversely, individuals with no epsilon 4 alleles may get AD.
- This study was designed to determine whether Apo E alleles could predict cognitive test performance in a normal, healthy population over a period of 14 years. Finding such a relationship might help to increase odds of accurate prediction of AD in later life.

Method

- Participants: were selected from the Seattle Longitudinal Study (SLS), and came from two age groups: Middle-aged participants averaged 47 years, and Older participants averaged 65 years of age. Both groups had slightly higher percentages of females than males, and the Middle-aged group had more education.

- Blood was drawn during a routine physical examination and analyzed to determine the Apo E allele combination possessed by each participant. The table below describes the distributions obtained within each age group.

	Middle-Age	Older
epsilon 2/2	2	1
epsilon 3/2	27	37
epsilon 3/3	138	166
epsilon 4/2	8	4
epsilon 4/3	52	54
epsilon 4/4	7	5

- Materials: All participants received a large battery of pencil-and-paper psychometric tests at each testing occasion (1984, 1991, and 1998).

- This study is concerned only with scores obtained on the five subtests of Thurstone's (1949) test of Primary Mental Abilities (PMA).

- The five cognitive domains measured were: Reasoning, Spatial orientation, Numeric ability, Verbal meaning, and Word fluency.

- Procedure: Tests were administered in small groups, using a trained tester and proctor, in familiar locations close to the homes of participants. Three waves of data from the SLS are considered: 1984, 1991, and 1998.

Design

- Repeated measures analyses of covariance (ANCOVAs), controlling for educational level, were employed to probe potential differences in performance that might be attributable to Apo E allele types.

Results

- Separate ANCOVAs were carried out for each of the five subtests of the Primary Mental Abilities test.
- ANCOVAs were 2 (age groups) x 5 (allele types) x 3 (occasions) factorial design, with education as covariate.
- Allele type had no significant main effect in any of the analyses.
- In the analysis on "Reason" subscores, a significant 3-way interaction occurred. Figures 1 and 2 depict the interaction space.
- A significant 2-way interaction was also observed on "Reason" scores, between allele type and occasion, as depicted in Figure 3. In light of the 3-way interaction above, the 2-way interaction is of little interest except in mimicking previous results obtained from a less age-diversified sample.
- Most importantly, sample sizes for the Apo E epsilon 4/4 and 4/2 groups were quite small. The results obtained are likely to be artifactual.

Conclusions

- Very small numbers of participants in our overall sample possessed the Apo E epsilon 4/4 or 4/2 allele combinations.
- Observed interactions, while statistically significant, may be the result of highly skewed distributions within the small sub-samples, or to random error in sampling.
- Thus, the present study appears to be insufficient for drawing inferences regarding the relation of the Apo E allele to cognitive performance in adults in mid to later life.
- Oversampling of populations of individuals possessing the more rare allele combinations is likely necessary in order to yield more definitive conclusions.
- Additionally, the results obtained by other researchers concurrently working in this area (see Small, et al., this session, for results from the Victoria Longitudinal Study) may shed additional light on this topic.

Figure 1:

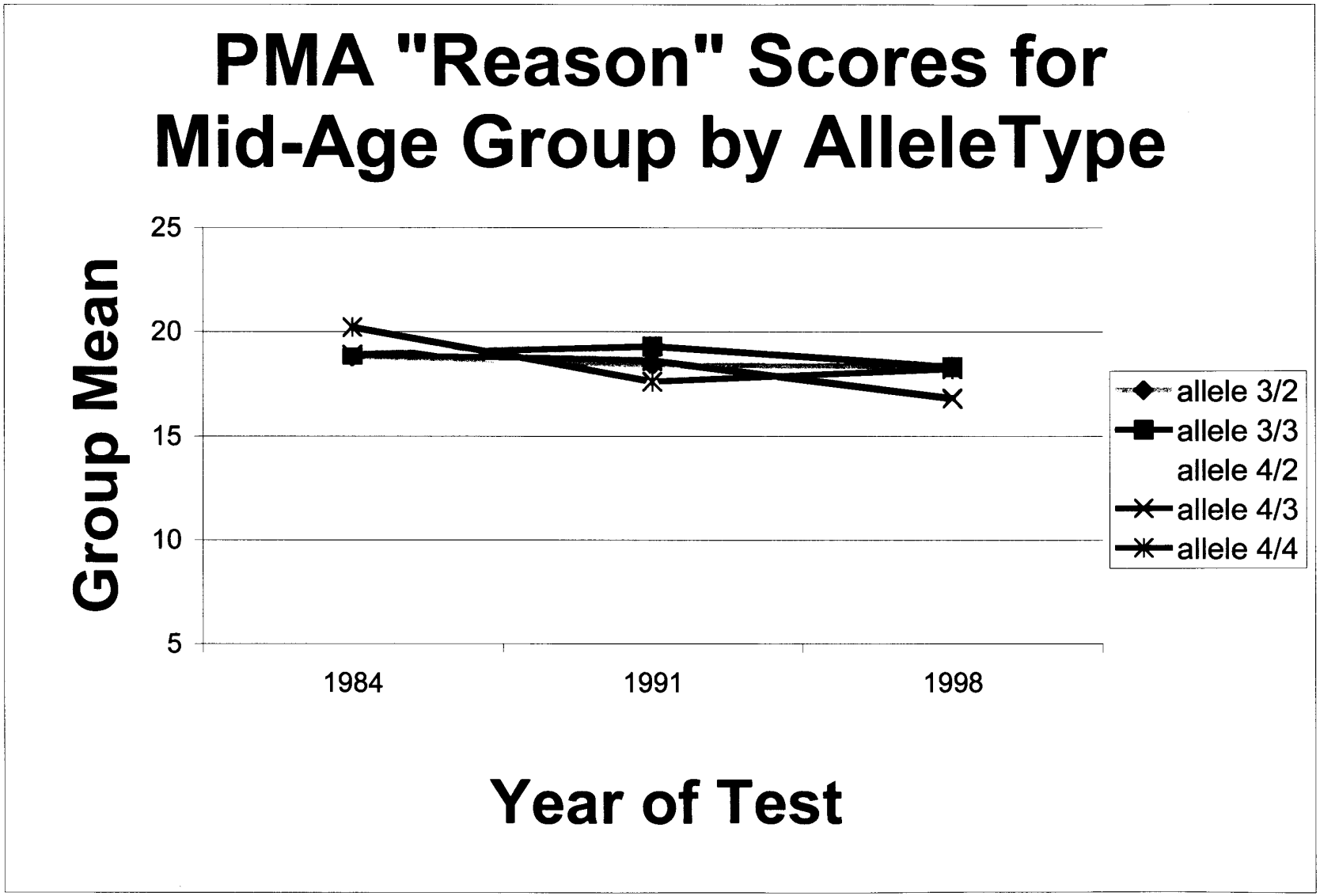
PMA "Reason" Scores for Mid-Age Group by AlleleType
Group Mean
25
20
15
10
5
1984
1991
1998
Year of Test
allele 3/2
allele 3/3
allele 4/2
allele 4/3
allele 4/4

Figure 2:

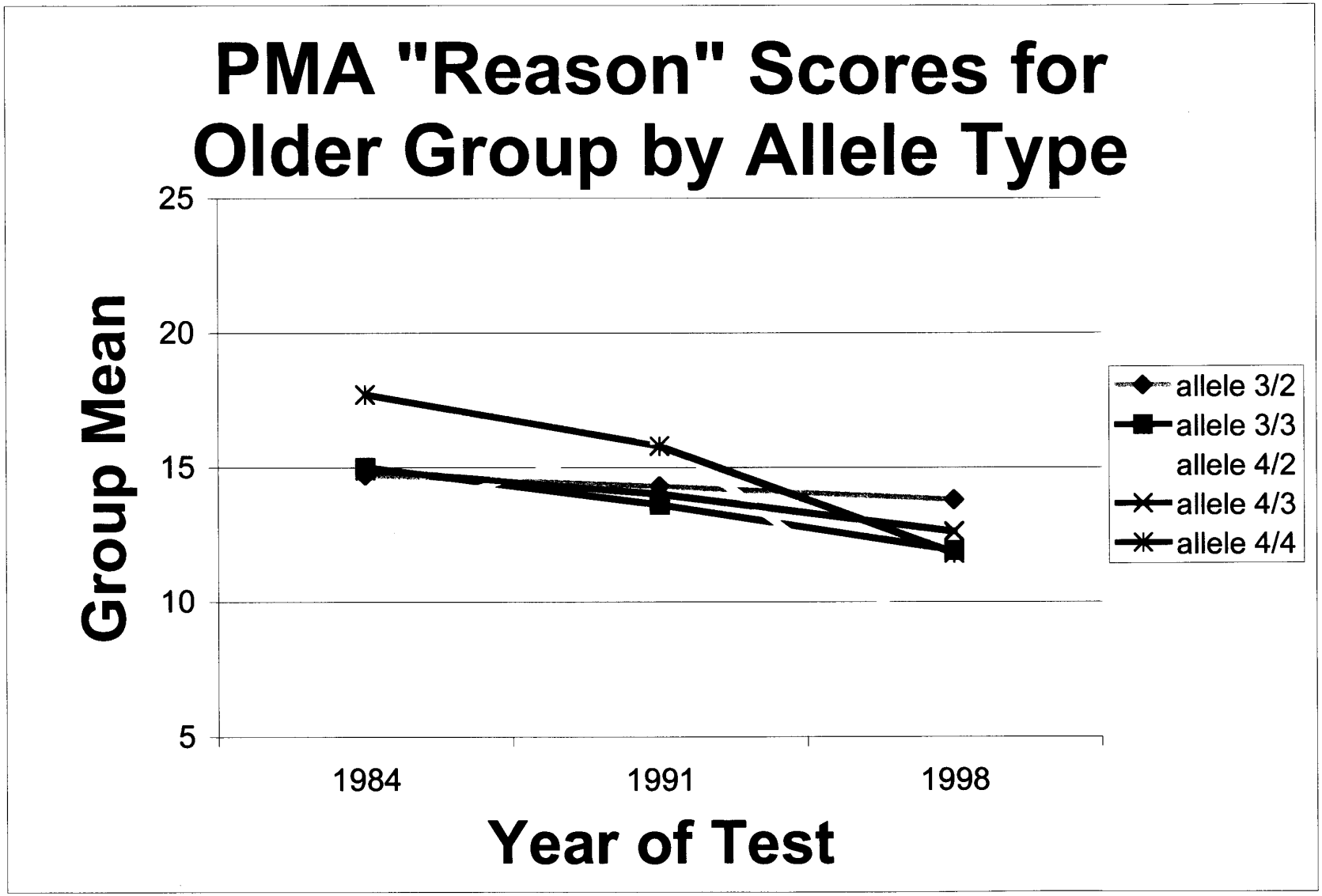
PMA "Reason" Scores for Older Group by Allele Type
Group Mean
25
20
15
10
5
1984
1991
1998
Year of Test
allele 3/2
allele 3/3
allele 4/2
allele 4/3
allele 4/4

Figure 3:

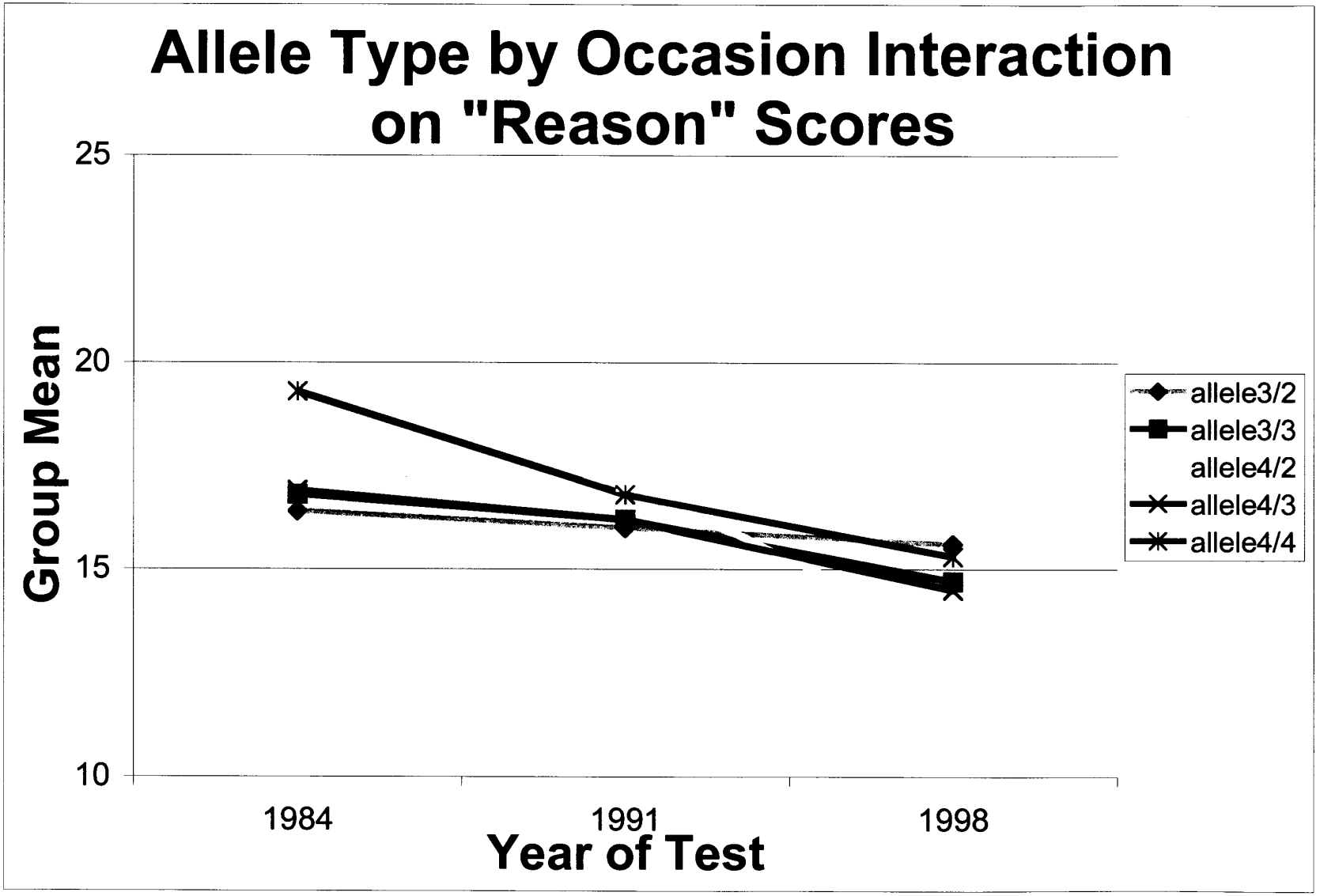
Allele Type by Occasion Interaction on "Reason" Scores
Group Mean
25
20
15
10
1984
1991
1998
Year of Test
allele3/2
allele3/3
allele4/2
allele4/3
allele4/4

Table 1: Standardized regression weights and associated t-values for variables potentially affecting recall.

Group	Occasion		Familiarity	Imageability	Primacy	Recency
Middle-Age	84	B	.34	.37	.63	.36
		t	1.98±	2.23*	3.93**	2.08±
	91	B	.26	.41	.67	.31
		t	1.50	2.59*	4.24***	1.83±
Young-Old	84	B	.42	.31	.56	.41
		t	2.23*	1.82±	3.27**	2.23*
	91	B	.43	.26	.57	.31
		t	2.42*	1.50	3.21**	1.66
Old-Old	84	B	.38	.23	.62	.28
		t	1.98±	1.29	3.53**	1.46
	91	B	.50	.23	.49	.22
		t	2.63*	1.30	2.81*	1.18
Females		B	.35	.36	.58	.31
		t	1.88±	2.08±	3.33**	1.66
Males		B	.49	.22	.59	.35
		t	2.74*	1.31	3.59**	1.98±

* $p < .05$ ** $p < .01$ *** $p < .001$ ± $.05 < p < .10$