

# Differential Declines in Cognitive Abilities for APOE Allele Types



## in the Seattle Longitudinal Study

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### ABSTRACT

This study examined differences in the rate of change of cognitive abilities for groups varying in APOE allele type. Risk for cognitive decline in old age has been found to vary by APOE allele type, where the APOE-ε4 allele is considered the second leading risk factor for Alzheimer's disease after age. The sample included three groups of participants from the Seattle Longitudinal Study (Total N = 1116; M age = 48.9); Homozygous ε4 (N = 26; M age = 50.7); Heterozygous ε4 (N = 284; M age = 48.5); no ε4 (N = 806; M age = 50.7). Rate of cognitive change over a 14 year period was examined for five primary mental abilities: inductive reasoning, spatial orientation, number, verbal, and word fluency. Change was also examined for three tests of cognitive styles (tests for behavioral rigidity): psychomotor speed, motor-cognitive flexibility, and attitudinal flexibility, as well as composite indexes of IQ (Intellectual Ability) and EQ (Educational Aptitude). The homozygous ε4-group had significantly greater decline in reasoning over fourteen years than the no ε4 group [F(1, 832) = 4.68, p < .05] and also significantly greater decline than the heterozygous group [F(1, 310) = 6.12, p < .05]. There were no mean differences in the rate of change in young adulthood (age 22-42) between groups differing in allele type. However, the homozygous ε4 group showed a substantially greater magnitude of decline in middle age (age 43-59) as compared to other allele groups.

### RESEARCH QUESTIONS

- 1) Does magnitude of change in Cognitive abilities (inductive reasoning, spatial orientation, number ability, verbal ability, and word fluency) vary by APOE allele type?
- 2) Do group differences in allele type vary in magnitude of ability change by age-group?
- 3) Does magnitude of change in cognitive style measured by Tests of Behavioral Rigidity (Psychomotor Speed, Motor-Cognitive Flexibility, and Attitudinal Flexibility) vary by APOE allele type?
- 4) Do differences in Cognitive composites: IQ and EQ vary by APOE allele type?

### PARTICIPANTS

- Sample participants are individuals from the Seattle Longitudinal Study who have been APOE genotyped (N = 1116) and have participated in longitudinal primary mental ability measures for at least two occasions (14-year period) from 1956 to 1998.
- Mean age for total sample = 48.9 (at occasion 1)
- Mean age homozygous ε4 = 50.7;
- Mean age for heterozygous ε4 = 48.5;
- Mean age for non-ε4 = 50.7;
- Demographic characteristics are shown in Table 2, Allelic frequencies are shown in Table 2.

### RESULTS

Table 1. Demographic char. for the entire sample (N = 1116).

Characteristic	Freq.
<u>Age-Group</u>	
22 to 42 years old	323
42 to 59 years old	533
60 years and older	266
<u>Sex Characteristics</u>	
Male ε4	128
Female ε4	184
Male no ε4	341
Female no ε4	470

Table 2. Fourteen year cognitive change by APOE allele type: Mean, magnitude of cognitive change and standard deviation.

Ability	APOE ε44	APOE ε24, ε34	APOE ε22, ε23, ε33
<u>Primary Mental Ability (PMA)</u>			
Inductive Reasoning	-1.69 (5.01)*	-0.01 (4.44)	-0.24 (5.10)
Number Ability	-1.27 (4.09)	-0.77 (5.42)	-0.85 (5.83)
Space Orientation	-1.07 (5.04)	-0.12 (6.33)	-0.47 (6.48)
Word Fluency	-0.85 (9.44)	0 (6.30)	-0.58 (6.25)
Verbal Meaning	0.65 (3.67)	0.08 (5.02)	0.25 (4.84)
<u>Cognitive Style (TBR)</u>			
Psychomotor Speed	2.38 (6.10)	1.36 (5.71)	1.52 (6.02)
Motor Cognitive Flexibility	-0.27 (6.56)	-0.54 (7.09)	-0.57 (7.57)
Attitudinal Flexibility	-0.96 (7.97)	0.29 (9.04)	0.04 (7.22)
<u>Composite Indexes</u>			
IQ	-1.19 (4.19)	-0.36 (3.55)	-0.57 (3.96)
EQ	0.04 (3.59)	0.06 (4.14)	0.13 (4.25)

Note: \* p < .05: Please note that the mean for APOE ε44 is significantly different from the mean of APOE ε24, ε34 AND APOE ε22, ε23, ε33 ONLY.

Table 3. Allelic Frequencies and mean years of education.

APOE Allele type	Freq.	Mean yrs. Educ. (S.D.)
22	8	11.75 (3.77)
23	148	14.62 (2.96)
24	40	15.15 (3.21)
33	655	14.83 (2.63)
34	245	14.96 (2.64)
44	26	15.42 (2.02)

### ANALYSES

- 14 Year Change scores created: Occasion 3 - Occasion 1.
- A series of MANCOVA comparisons while co-varying on education for 10 dependent variables: inductive reasoning, spatial orientation, number ability, verbal ability, word fluency, psychomotor speed, motor cognitive flexibility, attitudinal flexibility, IQ (Intellectual Ability) and EQ (Educational Aptitude). Dependent variables are magnitude of change across two occasions, within 14 years.
- Post-hoc comparisons were made to examine differences in magnitude of cognitive change by age-group and allele type.

### CONCLUSIONS

- MANCOVA comparisons indicated that there were significant differences in magnitude of change in reasoning ability by allele type. The homozygous ε4 group had significantly greater decline over this period than the heterozygous ε4 group and the non-APOE ε4 group. Reasoning ability declines may also implicate changes in working memory due to the high correlation between inductive reasoning and working memory.
- Participants grouped as APOE ε44 had a greater magnitude of decline over a 14 year period for 7 measures (number ability, inductive reasoning, word fluency, spatial orientation, Attitudinal Flexibility, Educational Aptitude composite and Intellectual Ability composite) as compared with APOE ε24 and ε34 individuals, and compared with non-APOE ε4 individuals.
- This research suggests that cognitive changes vary by APOE allele type, and these changes are highly domain specific. Furthermore, homozygous APOE ε4 individuals may be at a greater risk for cognitive decline than heterozygous APOE ε4 individuals. Also changes may be observable in Middle-age for individuals with genetic risk for late-onset Alzheimer's Disease.
- Based on these preliminary findings, it appears that crystallized abilities, such as verbal abilities are not declining across two occasions for those with the greatest APOE ε4 genetic risk.

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