Supplementary Material

Genetic Risk for Alzheimer's Disease Alters Perceived Executive Dysfunction in Cognitively Healthy Middle-Aged and Older Adults

INTRODUCTION

This study was not designed to evaluate perceived memory functioning. However, our participants did complete objective memory testing using the Rey Auditory Verbal Learning Test (RAVLT), and we administered the Geriatric Depression Scale (GDS), which includes the following question, "Do you feel you have more problems with memory than most? (yes/no)". We therefore performed a post-hoc analysis using these measures to compare subjective memory functioning (SMF) to our primary results with subjective executive functioning.

MEMORY FACTOR

Principal Components Analysis (PCA) was used to reduce the RAVLT scores (Trial 1, Trial 1to5 sum, immediate recall, delayed recall) to a single episodic memory factor score, comparable to what was used with executive functioning tests. The tests included were significantly intercorrelated ($|r| = 0.593$ to 0.867, all $p < 0.001$). All scores loaded on the factor at 0.83 to 0.95 (eigenvalue = 3.27); the model accounted for 82% of the variance.

DESCRIPTIVE STATISTICS

A summary of the memory variables is presented in Supplementary Table 1. Thirteen of 55 participants endorsed having more memory problems than most (24%); 11 of those 13 participants were ε4 non-carriers, reflecting 31% of non-carriers but only 11% of ε4 carriers. Given the relatively small sample, there was not a statistically significant difference between ε4 groups in subjective memory functioning endorsement ($\chi^2 = 2.48$, $p = 0.12$).

Supplementary Table 1. Descriptive statistics (mean (± SD)).

	Full Sample	***APOE* ε4+**	***APOE* ε4-**	***p***
	(n = 54)	(n =18)	(n = 36)	
AVLT Trial 1	6.13 (2.04)	6.16 (2.04)	6.11 (2.07)	0.78
AVLT Trials 1 to 5 (sum)	47.67 (9.96)	47.53 (11.51)	47.75 (9.22)	0.78
AVLT Immediate Recall	9.65 (3.10)	9.70 (3.17)	9.58 (3.10)	0.64
AVLT Delayed Recall	9.24 (3.69)	9.42 (3.63)	9.14 (3.77)	0.66
Episodic Memory Factor	0.00 (1.00)	0.104 (1.02)	-0.014 (0.99)	0.12
Memory SCC (yes/no)	0.24 (0.43)	0.11 (0.32)	0.31 (0.47)	0.69

AVLT, Rey Auditory Verbal Learning Test; SCC, subjective cognitive complaints.

INTERCORRELATIONS

Exploratory correlations are shown in Supplementary Table 2. Subjective memory functioning did not significantly correlate with other study variables. Objective memory performance (Memory Factor) significantly correlated with age and with objective executive functioning (EF_Factor). Subjective memory functioning correlated significantly with depression, but the perceived memory functioning measure is drawn from the same instrument. As such it was not considered a valid covariate.

Supplementary Table 2. Exploratory correlations.

All (n=54)	SMF	Age	Sex	*APOE* ε4	MMSE	Memory Factor
SMF						
Age	-0.27					
Sex	0.01	-0.08				
APOE ε4	-0.21	**0.35**	0.24			
MMSE	0.02	-0.06	0.04	0.18		
Memory Factor	-0.05	**-0.34**	-0.05	-0.21	0.06	
EXECDYS	0.25	-0.05	-0.23	-0.03	-0.25	
EF_Factor	-0.05	**-0.48**	-0.05	-0.23	0.06	**0.59**

Significant correlations ($p < 0.05$) are in **bold**; all correlations are Pearson r except with Memory SCC, sex, ε4 (Spearman rho); SMF, subjective memory functioning; EXECDYS, Frontal Assessment Battery executive dysfunction subscore (subjective executive functioning); *APOE*, Apolipoprotein E; MMSE, Mini-Mental State Exam total score; Memory Factor, factor score of objective memory testing; EF_Factor, factor score of objective executive functioning battery.

REGRESSION MODEL SUMMARY

None of the memory models were significant (there were no significant predictors at any step), including: a) with SMF as the outcome variable and objective executive functioning as the predictor and ε4 as the moderator; b) with SMF as the outcome, the episodic memory factor score as the predictor, and ε4 as the moderator; and c) with SEF (EXECDYS) as the outcome, the memory factor score as the predictor, and ε4 as the moderator. The latter analysis validates the specificity of the primary study results to executive functioning.

INTERPRETATION

There was a smaller proportion of ε4 carriers than non-carriers who endorsed memory concerns, which is slightly suggestive of anosognosia for memory. However, there was no significant correlation between perceived memory functioning and memory performance, nor was there a discrepancy between memory performance and memory concerns by ε4 group. Thus, comparing this analysis with the primary analyses, our findings in subjective executive dysfunction were more robust and thereby more sensitive to anosognosia in these cognitively intact elders. However, this conclusion remains speculative until future research is done to directly compare SCC in memory and executive functioning. At present it is uncertain whether memory concern was actually less robust than subjective executive dysfunction, or whether the post-hoc measure of memory concern used herein lacked sensitivity.