

## Short Communication

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# *APOE* $\epsilon 4$ Allele and Financial Capacity Performance in Mild Alzheimer's Disease: A Pilot Study

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Accepted 27 December 2020

Pre-press 23 January 2021

### Abstract.

This study aims to explore a little investigated topic, i.e., whether the presence of the *APOE*  $\epsilon 4$  allele in patients with a diagnosis of mild Alzheimer's disease (AD) can influence financial capacity. Twenty-eight elders with mild AD carrying the *APOE*  $\epsilon 4$  allele and 28 matched non-carrier patients were examined with an extensive battery of neuropsychological tests, and a specific test measuring financial capacity: Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS). The presence of the *APOE*  $\epsilon 4$  allele does not differentiate the group of mild AD patients regarding a number of cognitive domains necessary for financial capacity scores as measured by LCPLTAS.

Keywords: *APOE*  $\epsilon 4$ , financial capacity, mild Alzheimer's disease

## INTRODUCTION

The Apolipoprotein E (*APOE*)  $\epsilon 4$  allele is a major genetic risk factor for Alzheimer's disease (AD) both for early-onset and late-onset AD as well as familial and sporadic cases [1, 2]. Research conducted to date has demonstrated diminished performance of financial capacity in AD without examining the influence of genetic factors [3]. Not only AD, but also other forms of neurocognitive disorders, such as Parkinson's disease [4], vascular dementia [5], and amnesic mild cognitive impairment [6] have not been examined. Every individual has two copies of the gene and the combination of these copies determines the *APOE* genotype ( $\epsilon 2/\epsilon 2$ ,  $\epsilon 2/\epsilon 3$ ,  $\epsilon 2/\epsilon 4$ ,  $\epsilon 3/\epsilon 3$ ,  $\epsilon 3/\epsilon 4$ , and  $\epsilon 4/\epsilon 4$ ).

Significant negative associations have been found between the presence of the  $\epsilon 4$  allele and different cognitive domains including global cognitive function, memory, executive function, and information processing speed [7]. However, scarce data exist for the group of already diagnosed AD patients and their cognitive performance related to *APOE*  $\epsilon 4$  [8]. More specifically, this study aims to cover this knowledge gap regarding cognitive functioning by focusing on all related aspects of financial capacity, a neglected so far but complex cognitive capacity. Financial capacity includes a variety of activities and specific skills such as basic monetary skills, cash transactions, bank statement management, bill payment, financial conceptual knowledge, financial decision making, and knowledge of personal assets. These activities and skills are based on the abovementioned cognitive domains afflicted by *APOE*  $\epsilon 4$ . [3]. In this study, performance on financial capacity and subdomains is examined in two relevant groups, mild AD *APOE*

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ε4 carriers and mild AD *APOE* ε4 non-carriers with similar demographic characteristics.

## METHODS

Fifty-six Greek older adults (34 women, 22 men) participated in this study. Participants prior to enrolling to this study were examined following a common protocol in use in Papanikolaou Hospital. Diagnostic assessment consisted of medical history, standard assessment scales, physical examination, blood samples, and structural imaging (computerized tomography and/or magnetic resonance imaging). The diagnosis of AD was made prior to the enrollment according to National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ARDA) by a trained geriatric neurologist. The neuropsychological assessment was completed during a pre-arranged visit at the Memory Clinic of Papanikolaou General Hospital and elderly day care centers. Next, the participants underwent an additional laboratory blood analysis for *APOE* genotype. The patients with a diagnosis of mild AD were divided in two groups: the control (ε4 non-carriers) and experimental (ε4 carriers) groups, which were matched in age [ $T(54) = 1.015$ ,  $p = 0.315$ ], gender (equally 28 men and women were distributed in the two groups), and years of education [ $T(54) = 0.018$ ,  $p = 0.986$ ] in order to eliminate the influence of these variables as possible confounders. The age for the mild AD *APOE* ε4 carriers' group was  $M = 73.67$ ,  $SD = 6.78$ , and for the mild AD *APOE* ε4 non-carriers was  $M = 73.60$ ,  $SD = 8.39$ , while the education in years for the mild AD *APOE* ε4 carriers' group was  $M = 7.51$ ,  $SD = 3.72$ , and for the mild AD *APOE* ε4 non-carriers was  $M = 7.50$ ,  $SD = 3.87$ . Both groups had the same level of prior involvement with financial matters in their life as young adults (before the first symptoms of the disease), according to a brief interview with their caregivers (spouses and children). Subjects had a score of more than 4 in a 5-point Likert scale question asking whether they had managed successfully and alone their everyday financial affairs, a question that was also answered by their caregivers who accompanied them during the assessment meetings. Regarding their genetic *APOE* testing,  $n = 6$  had ε2/ε3,  $n = 22$  had ε3/ε3,  $n = 21$  had ε3/ε4,  $n = 2$  had ε2/ε4, and  $n = 5$  had ε4/ε4 but at the time of the neuropsychological assessment the patients, their family members

as well the examiner were not aware of the genetic test results.

A detailed neuropsychological battery covering a variety of cognitive areas was administered, including Mini-Mental State Examination (MMSE) [9], Test of Everyday Attention [10], Trail Making Test-Parts A and B [11], Rey-Osterrieth Complex Figure Test-copy condition and immediate and delayed recall conditions of the complex design [12], Rey Auditory Verbal Learning Test [13], Rivermead Behavioural Memory Test [14], Verbal Fluency Task [15], Neuropsychiatric Inventory [16], Instrumental Activities of Daily Living [17], Clinical Dementia Rating [18], and Functional-Cognitive Assessment Scale [19]. In addition to that, the Geriatric Depression Scale-15 (GDS-15) was used with a cutoff score of at least six to exclude individuals with depressive symptomatology [20].

Financial capacity was assessed with the Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS) [3]. LCPLTAS is culturally adapted for the Greek everyday financial reality and it consists of a total of seven domains, namely 1) basic monetary skills, 2) cash transactions, 3) bank statement management, 4) bill payment, 5) financial conceptual knowledge, 6) financial decision making, and 7) knowledge of personal assets. The LCPLTAS contains some items in the form of tasks, while some others are presented in the form of a semi-structured interview. For each question or task there is only one correct answer [3].

Participants were excluded as in similar studies [3–6] when the following criteria were present: a recorded history of stroke, a history of substance abuse, previous traumatic brain injury and related neurosurgical interventions, concomitant serious medical illness (significant visual and/or auditory impairment not corrected sufficiently by visual/auditory aids, a history of other neurologic or psychiatric disorder that may interfere with the patient's neuropsychological performance).

Informed consent was obtained from all participants prior to their admission to the study and after a detailed description of the procedure. The study was approved by the Ethics Committee of the Aristotle University of Thessaloniki (as part of a larger study [3]) following the declaration of Helsinki.

Independent samples *t*-tests were performed with two comparison groups (mild AD *APOE* ε4 carriers and mild AD *APOE* ε4 non-carriers) and regarding MMSE and LCPLTAS scores. Probability values  $< 0.05$  were considered statistically significant.

**RESULTS**

When comparisons were made between mild AD *APOE ε4* carriers and mild AD *APOE ε4* non-carriers, no statistically significant differences were found for MMSE scores [T(54)=0.405, *p*=0.687, Glass’s Δ=0.09], GDS [T(54)=0.554, *p*=0.582, Glass’s Δ=0.19], but also the financial capacity as examined by LCPTLAS total score [T(54)=0.048, *p*=0.962, Glass’s Δ=0.01] and the relevant subscales of LCPTLAS; basic monetary skills [T(54)=0.428, *p*=0.671, Glass’s Δ=0.10], cash transactions [T(54)=0.312, *p*=0.756, Glass’s Δ=0.07], bank statement management [T(54)=0.108, *p*=0.914, Glass’s Δ=0.02], bill payment [T(54)=0.522, *p*=0.604, Glass’s Δ=0.12], financial conceptual knowledge [T(54)=0.242, *p*=0.810, Glass’s Δ=0.06], financial decision making [T(54)=0.171, *p*=0.865, Glass’s Δ=0.04], and knowledge of personal assets [T(54)=0.026, *p*=0.979, Glass’s Δ=0.06] (see Table 1).

In addition, nonparametric bootstrapped estimates of the 95% confidence intervals for mean difference were made. The procedure involved sampling with replacement (1,000 samples of 56 cases) from the original data [21]. The results are shown in Table 2, where all estimates do span the zero point, which suggests not rejecting the null hypothesis.

**DISCUSSION**

One critical, and commonly overlooked, feature of the *APOE* link to AD is that so far financial performance has been neglected in systematic testing. Although it has been supported that it may be a wise choice to perform the *APOE* genetic testing for the diagnosis of AD in elders with poor performance in a screening test and a family history of dementia [22], the above findings provide support that when detailed neuropsychological testing is performed, financial

incapacity in mild AD is not influenced for *APOE ε4* gene carriers and non-carriers. It is imperative, at this point to make an epistemological annotation about the *reductionism* existing behind the stated hypothesis, that is whether and in what sense cognition can be reduced to genetics. This is a perpetual debate and an open issue [23], on which it is hard to draw causal interpretations. However, literature often brings about relevant issues, and it is worth probing and conversing about them [24]. The present study contributes to this issue by providing empirical counter evidence for supporting a direct relationship between the *APOE ε4* allele in AD and the performance in a relevant financial capacity empirical test, although the *APOE ε4* allele has been found to be linked to poorer cognitive performance in the domains of memory and processing speed in old age [25]. This evidence has to be taken into consideration

Table 1

Mean scores and SDs of MMSE, GDS and LCPTLAS total score and subscales in mild AD for *APOE ε4* gene carriers and non-carriers

Basic cognitive domains	<i>APOE ε4</i>	N	M	SD
MMSE	non-carrier	28	17.32	8.91
	carrier	28	18.17	6.77
GDS	non-carrier	28	1.96	2.51
	carrier	28	2.46	4.05
Total score LCPTLAS	non-carrier	28	84.67	77.83
	carrier	28	83.75	67.42
Subscales LCPTLAS	non-carrier	28	5.96	5.38
	carrier	28	5.39	4.58
Cash transactions	non-carrier	28	2.42	2.76
	carrier	28	2.64	2.36
Statement management	non-carrier	28	2.25	2.70
	carrier	28	2.17	2.22
Bill payment	non-carrier	28	2.78	3.02
	carrier	28	3.17	2.59
Conceptual knowledge	non-carrier	28	12.78	12.01
	carrier	28	13.53	11.18
Decision making	non-carrier	28	45.21	42.64
	carrier	28	43.39	36.94
Assets knowledge	non-carrier	28	13.25	10.98
	carrier	28	13.32	9.40

Table 2  
Results from bootstrap estimations for independent samples *t*-tests

Financial capacity subdomains	Statistic	Bias	Std. error	95% Confidence Interval	
				Lower	Upper
Basic monetary skills	0.57143	0.03114	1.35729	-2.17154	3.39357
Cash transactions	-0.21429	0.05352	0.69016	-1.51177	1.17857
Statement management	0.07143	-0.03594	0.64834	-1.30208	1.29021
Bill payment	-0.39286	0.01616	0.75222	-1.86819	1.07482
Conceptual knowledge	-0.75000	-0.05499	3.12678	-6.97368	5.44930
Decision making	1.82143	0.07814	10.31696	-18.79150	22.46268
Assets knowledge	-0.07143	-0.01546	2.71478	-5.49673	5.41517

as there is a widely accepted influence (in the bibliography related to cognition and genetics) of a plethora of other hypothesized mediating factors (e.g., socioeconomic factors) [26].

One of the major limitations of our study is the small sample size. Given that this is the first study of its kind to show that APOE ε4 has no differentiating power on financial capacity performance in the group of mild AD patients, future research could include larger samples [27, 28] and different stages and types of neurocognitive disorders in old age.

## ACKNOWLEDGMENTS

The authors would like to thank Olymbia Gatzima for her assistance in genetic analyses.

## CONFLICT OF INTEREST

The authors have no conflict of interest to report.

## REFERENCES

- [1] Chartier-Harlin MC, Parfitt M, Legrain S, Pérez-Tur J, Brousseau T, Evans A, Berr C, Vidal O, Roques P, Gourlet V, Fruchart J-C, Delacourte A, Rossor M, Amouyel P (1994) Apolipoprotein E, epsilon 4 allele as a major risk factor for sporadic early and late-onset forms of Alzheimer's disease: Analysis of the 19q13.2 chromosomal region. *Hum Mol Genet* **3**, 569-574.
- [2] Strittmatter WJ, Saunders AM, Schmechel D, Pericak-Vance M, Enghild J, Salvesen JS, Roses AD (1993) Apolipoprotein E: High avidity binding to beta-amyloid and increased frequency of type 4 allele in late onset familial Alzheimer disease. *Proc Natl Acad Sci USA* **90**, 1977-1981.
- [3] Giannouli V, Stamovlasis D, Tsolaki M (2018) Exploring the role of cognitive factors in a new instrument for elders' financial capacity assessment. *J Alzheimers Dis* **62**, 1579-1594.
- [4] Giannouli V, Tsolaki M (2019) Depression and financial capacity assessment in Parkinson's disease with dementia: Overlooking an important factor?. *Psychiatriki* **30**, 66-70.
- [5] Giannouli V, Tsolaki M (2020) Vascular dementia, depression and financial capacity assessment. *Alzheimer Dis Assoc Disord*, doi: 10.1097/WAD.0000000000000374
- [6] Giannouli V, Tsolaki M (2020) Unraveling Ariadne's thread into the labyrinth of aMCI: Depression and financial capacity. *Alzheimer Dis Assoc Disord*, doi: 10.1097/WAD.0000000000000417
- [7] Wisdom NM, Callahan JL, Hawkins KA (2011) The effects of apolipoprotein E on non-impaired cognitive functioning: A meta-analysis. *Neurobiol Aging* **32**, 63-74.
- [8] Giannouli V, Tsolaki M (2015) Financial capacity and dementia: To be or not to be an APOE e4 carrier. *Hell J Nucl Med* **S16**, 281.
- [9] Fountoulakis KN, Tsolaki M, Chantzi H, Kazis A (2000) Mini Mental State Examination (MMSE): A validation study in Greece. *Am J Alzheimers Dis Other Demen* **15**, 342-345.
- [10] Tsolaki M, Kounti F, Petkari E (2004) Attention disorders in normal elders, elders with mild cognitive impairment and patients with Alzheimer's disease. *J Hell Psychol Soc* **11**, 553-570.
- [11] Vlahou CH, Kosmidis MH (2002) The Greek Trail Making Test: Preliminary norms for clinical and research use. *J Hell Psychol Soc* **9**, 336-352.
- [12] Kounti F, Tsolaki M, Eleftheriou M (2004) The administration of Rey Complex Figure Test to Greek healthy, mildly cognitively impaired and demented elderly. Paper presented at the *1st International Conference on Quality of Life and Psychology*, Thessaloniki.
- [13] Kounti F, Tsolaki M, Nikolaides E (2004) The administration of Rey Auditory Verbal Learning test to Greek healthy, mildly cognitively impaired and demented elderly. Paper presented at the *1st International Conference on Quality of Life and Psychology*, Thessaloniki.
- [14] Efkliides A, Yiultsi E, Kangelidou T, Kounti F, Dina F, Tsolaki M (2002) Wechsler Memory Scale, Rivermead Behavioral Memory Test, and Everyday Memory Questionnaire in healthy adults and Alzheimer patients. *Eur J Psychol Assess* **18**, 63-77.
- [15] Kosmidis MH, Vlahou CH, Panagiotaki P, Kiosseoglou G (2004) The verbal fluency task in the Greek population: Normative data and clustering and switching strategies. *J Int Neuropsychol Soc* **10**, 164-172.
- [16] Politis AM, Mayer LS, Passa M, Maillis A, Lyketsos CG (2004) Validity and reliability of the newly translated Hellenic Neuropsychiatric Inventory (H - NPI) applied to Greek outpatients with Alzheimer's disease: A study of disturbing behaviors among referrals to a memory clinic. *Int J Geriatr Psychiatry* **19**, 203-208.
- [17] Theotoka I, Kapaki E, Vagenas V, Ilias I, Paraskevas GP, Liappas I (2007) Preliminary report of a validation study of Instrumental Activities of Daily Living in a Greek sample. *Percept Mot Skills* **104**, 958-960.
- [18] Morris JC (1993) The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology* **43**, 2412-2414.
- [19] Kounti F, Tsolaki M, Kiosseoglou G (2006) Functional Cognitive Assessment Scale (FUCAS): A new scale to assess executive cognitive function in daily life activities in patients with dementia and mild cognitive impairment. *Hum Psychopharmacol* **21**, 305-311.
- [20] Fountoulakis KN, Tsolaki M, Iacovides A, Yesavage J, O'Hara R, Kazis A, Ierodiakonou C (1999) The validation of the short form of the Geriatric Depression Scale (GDS) in Greece. *Aging Clin Exp Res* **11**, 367-372.
- [21] Efron B, Tibshirani R (1993) *An Introduction to the Bootstrap*. Chapman & Hall, New York.
- [22] Yang HJ, Kang NR, Jung YE, Kim MD, Jeong HG, Lee TJ, Han JW, Kim KW, Park JH (2020) "Choosing Wisely": Apolipoprotein E genetic testing for the diagnosis of Alzheimer's Disease in dementia clinics. *J Alzheimers Dis* **74**, 1253-1260.
- [23] Plomin R (1999) Genetics and general cognitive ability. *Nature* **402**, C25-C29.
- [24] Ding X, Barban N, Tropf FC, Mills MC (2019) The relationship between cognitive decline and a genetic predictor of educational attainment. *Soc Sci Med* **239**, 112549.
- [25] Marioni RE, Campbell A, Scotland G, Hayward C, Porteous DJ, Deary IJ (2016) Differential effects of the APOE e4

allele on different domains of cognitive ability across the life-course. *Eur J Hum Genet* **24**, 919-923.

- [26] Tucker-Drob EM, Briley DA, Harden KP (2013) Genetic and environmental influences on cognition across development and context. *Curr Dir Psychol Sci* **22**, 349-355.
- [27] Giannouli V (2018) Elder abuse and consent capacity: Our collective nemesis?. In *Social, Psychological, and Forensic*

*Perspectives on Sexual Abuse*, Gopalan RT, ed. Medical Information Science Reference, Hershey, PA, pp. 207-221.

- [28] Giannouli V, Tsolaki M (2014) Legal capacity of the elderly in Greece. *Hell J Nucl Med* **17**, 2-6.