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REGULAR ARTICLE

Liberating older adults from the bonds of vascular risk factors: What is their impact on financial capacity in amnestic mild cognitive impairment?

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Background: There is a pressing need to clarify whether vascular risk factors (VRFs) are related to the heterogeneous cognitive performance found in mild cognitive impairment (MCI) and whether the number of VRFs relates to financial capacity impairment in patients with amnestic MCI (aMCI).

Methods: A total of 112 participants were divided into three groups: patients with single-domain aMCI, patients with multiple-domain aMCI, and healthy controls (HCs), while taking into consideration whether participants had a diagnosis of one VRF or disease, or more than one VRF or disease. Patients with aMCI with VRFs (one and more than one VRF) and HCs did not differ significantly in age, education, and sex. Mini-Mental State Examination, 15-item Geriatric Depression Scale, and Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS) were administered to all groups.

Results: Diagnosis (P <0.001) and VRFs (P = 0.006) showed significant main effects on LCPLTAS but no interaction (P = 0.654). Patients with aMCI with high vascular burden were more frequently of the multiple-domain subtype, whereas patients with no vascular burden were more frequently of the single-domain subtype. A larger vascular burden is correlated with lower LCPLTAS scores.

Discussion: Vascular burden plays an important role in the heterogeneity of aMCI by impairing financial capacity.

Keywords: *aMCI, cognitive function, financial capacity, vascular risk factors.*

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Introduction

Increasing evidence supports the important role of diagnosis and treatment of vascular risk factors (VRFs) in prevention attempts regarding cognitive decline and dementia.[1] In this line, there is a recorded reappraisal of VRFs and their negative impact on cognitive functioning in middle-aged and older adults, which is focused mainly on the most common VRFs, ie, hypertension, hypercholesterolemia, diabetes mellitus, obesity, sedentary lifestyle, and tobacco use.[2] Some longitudinal studies have found significant associations between hypertension, diabetes, and metabolic syndrome (as assessed at middle age), and dementia,[3] but studies assessing the link between hypercholesterolemia, atrial fibrillation, former (not current) smoking, and dementia have given more conflicting results, by not supporting this negative correlation.[3,4] Furthermore, some studies have highlighted the possible protective effect of antihypertensive therapy on cognition.[4] In community-based older-aged 75-year-old individuals, other studies have reported no effects of VRFs (blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, glycated hemoglobin, homocysteine, lipoprotein(a), fibrinogen, C-reactive protein, and smoking habits) on overall cognition as measured by the Mini-Mental State Examination (MMSE), although pathological VRFs were found frequently in this age cohort.[5]

Financial capacity is a complex capacity relating to instrumental activities of daily living that allows an individual to live independently in a community,[6,7] but it is also related to cognitive capacities such as arithmetic skills[8] and executive functioning.[9] Financial capacity comprises a variety of skills, including performance skills (such as arithmetic counting coins/currency and paying bills) and judgment–decision-making skills.[6,7] Financial capacity so far has been examined in patients with Parkinson disease,[10] multiple-domain aMCI,[11] frontotemporal dementia,[12] vascular dementia[3] and mild Alzheimer disease.[14] All of these studies support that depression has detrimental effects on financial capacity,[10–14] but other studies also support the influence of additional factors such as psychological (apathy),[15] biological (left angular gyrus and amygdala brain volumes),[16] and educational (literacy) aspects,[17] but not genetic (APOE ϵ4 gene) aspects[18] or cerebrospinal fluid biomarkers (amyloid β peptide 1–42, total tau, and phosphorylated tau concentrations).[19]

Taking into consideration previous studies showing that vascular burden and, more specifically, the number of multiple VRFs and diseases increase the amount of executive impairment in patients with aMCI similar to what has been repeatedly reported in healthy older adults,[20–22] this study aims to elucidate whether the two subtypes of aMCI,[23] ie, patients with single-domain aMCI who experience only isolated memory deficit and patients with multiple-domain aMCI who experience memory deficits plus deficits in other cognitive domains, most often executive, first present with the same frequency of VRFs, and second whether financial capacity can be affected by the cumulative effects of multiple VRFs in the two subtypes of aMCI.

Methods

The sample comprised a total of 112 older adults, Greek native speakers (21 men, 91 women). Their age ranged from 54 to 89 years (mean = 68.34, SD = 7.13 years). There were three groups: (i) patients with single-domain aMCI (n = 41, 10 men and 31 women; mean age = 68.31 years, SD = 7.85 years); (ii) patients with multiple-domain

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aMCI (n = 41, 4 men and 37 women; mean age = 68.63 years, SD = 6.90 years); and (iii) healthy controls (HCs) (n = 30, 7 men and 23 women; mean age = 68.00 years, SD = 6.62 years).

Participants were matched with the aMCI patient groups in age (F [2, 111] = 0.068, P = 0.934), sex ($\chi^2(2)$ = 3.447, P = 0.178), and years of education (F[2, 111] = 1.075, P = 0.345) in order to eliminate possible influences of the above-mentioned variables as confounders.

It should be clarified that participants in all groups were screened for depressive symptoms by using the 15-item Geriatric Depression Scale (GDS-15),[24] and those persons who scored above six were excluded from the study.

Vascular burden in all participants was measured by a questionnaire that was administered to them (which was also verified by their accompanying family members), along with a demographics questionnaire, and reported the risk factors (hypertension, hypotension, dyslipidemia, and diabetes) and diseases (carotid stenosis, history of coronary artery disease, transient cerebral ischemia, and cardiac arrhythmia). VRFs in patient groups and HCs were assessed according to their hematologic check of the past year, while all participants were nonsmokers at the time of the examination (n = 93) and/or reporting continuous abstinence for at least 1 decade (n = 19). Therefore, the three most common VRFs reported were: (i) hypertension (n = 64), (ii) hyperlipidemia (n = 42), and (iii) diabetes (n = 12), and were under medical supervision and medication. HCs were recruited from a pool of volunteers living in Northern Greece who underwent the same clinical and neuropsychological evaluation as the other groups. They were only included in this study if they performed within norms on cognitive tests (scores that did not reach the cutoff of 1.5 SD below normative values). For a detailed account of the neuropsychological tests see.[6]

Exclusion criteria for HCs were similar to those used in other neuropsychological protocols[25] and comprised: (i) a diagnosis of MCI or dementia of any type (or minor and/or major neurocognitive disorder according to *DSM-5* as the initial diagnosis and actual examination of participants was made in 2015 and the data were reexamined in retrospect according to the new diagnostic criteria); (ii) affective disorders such as depression or anxiety, as that could affect the validity of the diagnosis; (iii) epilepsy history, Parkinson disease, encephalitis, brain tumor, stroke history, and other neurological disorders such as hydrocephalus; (iv) cancer, myocardial infarction, pacemaker, and/or bypass; (v) history of schizophrenia, substance abuse, alcoholism, or psychiatric illness with and without hospitalization; (vi) prescribed medications (typical or atypical, antipsychotics, antidepressants, and benzodiazepines); and (vii) a history of traumatic brain injury.

Patients with aMCI came from the Memory Clinic of Papanikolaou General Hospital and "Alzheimer Hellas" centers in Thessaloniki, Greece. Patients had been diagnosed at least 6 months before and followed relevant medical instructions. The inclusion criteria for the aMCI group comprised a diagnosis of minor neurocognitive disorders according to *DSM-5* criteria and neurological evaluation, validating the diagnosis (as initial examination data were reexamined according to the new criteria). The diagnosis of aMCI was supported by an extensive neurological, neuropsychological, and neuropsychiatric evaluation; neuroimaging, such as computed tomography and/or magnetic resonance imaging; and routine blood tests or serum tests to identify biological markers or risk genes. MCI and its subtypes, in particular, were diagnosed according to the Petersen criteria,[23] and more specifically a self- and/or informant report regarding memory complaints for ≥6 months, and objective cognitive impairment especially in the memory domain based on observed neuropsychological test scores generally falling 1.5 SDs below appropriate Greek norms. The exclusion criterion was a diagnosis of major neurocognitive disorder according to *DSM-5* and all criteria mentioned for the previously presented group of HCs regarding comorbid psychiatric/neurological disorders.

The neuropsychological tests that were administered included: the MMSE, Functional Cognitive Assessment Scale, Functional Rating Scale for Symptoms of Dementia, Trail Making Test-Parts A and B, Rey-Osterrieth Complex Figure Test (copy, immediate, and delayed recall conditions), Rey Auditory Verbal Learning Test, Boston Naming Test, Rivermead Behavioral Memory Test, Digit Span forward and backward, Wechsler Adult Intelligence Scale-Revised digit symbol substitution test, Neuropsychiatric Inventory, and Geriatric Depression Scale-15 (GDS-15).[6]

This detailed neuropsychological battery covering a variety of cognitive areas and assessment of mood was administered as stated above, with an emphasis on MMSE scores (as this specific test is found to be of importance for financial capacity[6]) along with other neuropsychological tests used in older age assessment in Greece.[6] The testing protocol took an average of 2 hours to complete. Financial capacity was assessed with the Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS) full form.[6] LCPLTAS is a standardized financial capacity tool developed in Greece. It is designed to evaluate seven subdomains of financial capacity: (i) basic monetary skills, (ii) cash transactions, (iii) bank statement management, (iv) bill payment, (v) financial conceptual knowledge, (vi) financial decision-making, and (vii) knowledge of personal assets.[6] This neuropsychological test contains some items/questions in the form of tasks and some others in the form of a semistructured interview. In this way it assesses different aspects of financial capacity of varying difficulty level organized into the abovementioned subdomains.[6] Therefore, some of the LCPLTAS tasks can be characterized as requiring simple (e.g. counting currency) or complex (e.g. taking financial decisions) knowledge or skills. LCPLTAS shows excellent internal, inter-rater and test–retest reliabilities.[6] Tasks are presented serially by domain, regardless of the individual's performance, beginning with subdomain (i) basic monetary skills, and ending with subdomain (vii) knowledge of personal assets.[6] The total score of the full version ranges from zero to 212 points.

All study participants provided written informed consent before their admission to the study, and, in cases that the older adults could not give consent themselves, their caregivers provided consent after a detailed description of the procedure. The research ethics committee of the Aristotle University of Thessaloniki School of Medicine approved the study (2/27.3.2013), and all research procedures were performed following the principles of the Declaration of Helsinki.

Statistical analysis

One-way ANOVA and chi-square test were used to determine whether patients with single-domain aMCI, those with multiple-domain aMCI,

Table 1. Means and SDs for the MMSE among the diagnostic groups and VRFs

Diagnosis of disease	VRF	Mean	SD
Single-domain aMCI	Zero	28.77	0.83
	One	27.60	1.11
	Two or more	26.55	1.23
	Total	27.63	1.29
Multiple-domain aMCI	Zero	27.00	0.00
	One	26.85	1.46
	Two or more	26.25	1.48
	Total	26.39	1.44
Healthy controls	Zero	29.13	0.43
	Total	29.13	0.43
Total sample	Zero	28.95	0.70
	One	27.43	1.22
	Two or more	26.31	1.42
	Total	27.58	1.60

aMCI, amnestic mild cognitive impairment; MMSE, Mini-Mental State Examination; VRF, vascular risk factor.

Table 2. Bonferroni correction for post hoc multiple comparisons regarding MMSE in the three diagnostic groups

(I) 1 = single aMCI 2 = multiple aMCI 3 = healthy	(J) 1 = single aMCI 2 = multiple aMCI 3 = healthy	Mean difference (I–J)	SE	*P*-value	95% CI	
					Lower bound	Upper bound
1	2	1.2439*	0.24724	0.000	0.6424	1.8454
	3	−1.4992*	0.26895	0.000	−2.1535	−0.8448
2	1	−1.2439*	0.24724	0.000	−1.8454	−0.6424
	3	−2.7431*	0.26895	0.000	−3.3974	−2.0887
3	1	1.4992*	0.26895	0.000	0.8448	2.1535
	2	2.7431*	0.26895	0.000	2.0887	3.3974

The error term is mean square (error) = 1.253. aMCI, amnestic mild cognitive impairment; CI, confidence interval; MMSE, Mini-Mental State Examination.
*The mean difference is significant at the 0.05 level.

Table 3. Bonferroni correction for post hoc multiple comparisons regarding MMSE in the three VRF groups

(I) VRF	(J) VRF	Mean difference (I–J)	SE	*P*-value	95% CI	
					Lower bound	Upper bound
0	1	1.5179*	0.26895	0.000	0.8635	2.1722
	2	2.6341*	0.24724	0.000	2.0326	3.2357
1	0	−1.5179*	0.26895	0.000	−2.1722	−0.8635
	2	1.1163*	0.26895	0.000	0.4619	1.7706
2	0	−2.6341*	0.24724	0.000	−3.2357	−2.0326
	1	−1.1163*	0.26895	0.000	−1.7706	−0.4619

The error term is mean square (error) = 1.253. CI, confidence interval; MMSE, Mini-Mental State Examination; VRF, vascular risk factor.
*The mean difference is significant at the 0.05 level.

and HCs differed on sociodemographic characteristics and on the index of vascular burden. Kendall correlations computed between the index of vascular burden and MMSE as well as LCPLTAS scores. Nonparametric correlations were performed because the distribution of the vascular burden was not normal and more specifically Kendall tau was selected as one variable was ordinal (VRFs) and the other two were continuous (MMSE and LCPLTAS scores). Moreover, a two-way ANOVA was conducted that included the between-patient factor vascular burden (three levels: zero VRF or disease [$n = 41$], one VRF or one disease [$n = 30$], and more than one VRF or disease [$n = 41$]), as well as diagnosis group (single-domain aMCI, multiple-domain aMCI, and HCs) to assess whether the combined effect of several VRFs and diseases amplified the cognitive deficit associated with vascular burden in patients with aMCI. Mean comparisons were then performed with Bonferroni post hoc tests with a 95% confidence level.

Results

According to chi-square test, there was a difference in VRF levels in the three groups of participants ($\chi^2[4] = 101.868$, $P < 0.001$). More specifically, individuals with single-domain aMCI presented with zero ($n = 9$), one ($n = 23$), and more than one VRF ($n = 9$). Individuals with multiple-domain aMCI presented with zero ($n = 2$), one ($n = 7$), and more than one VRF ($n = 32$), while HCs aMCI presented with zero ($n = 30$), one ($n = 0$), and more than one VRF ($n = 0$).

The results of the correlational analyses between the index of vascular burden in patients with aMCI showed that there was a significant negative correlation in aMCI between vascular burden and MMSE ($\tau = -0.648$, $P < 0.001$), two-tailed, as well as between the vascular burden and LCPLTAS ($\tau = -0.695$, $P < 0.001$). The correlations indicate that larger burden indices were associated with lower

Table 4. Means and SDs for LCPLTAS among diagnostic groups and VRFs

Diagnosis of disease	VRF	Mean	SD
Single-domain aMCI	Zero	195.42	3.99
	One	189.13	19.60
	Two or more	167.12	24.58
	Total	185.56	21.13
Multiple-domain aMCI	Zero	132.00	7.07
	One	124.42	9.23
	Two or more	113.12	30.99
	Total	115.97	28.11
Healthy controls	Zero	211.33	1.21
	Total	211.33	1.21
Total sample	Zero	204.41	18.26
	One	173.51	33.17
	Two or more	123.92	36.74
	Total	166.30	45.97

aMCI, amnestic mild cognitive impairment; LCPLTAS, Legal Capacity for Property Law Transactions Assessment Scale; VRF, vascular risk factor.

Table 5. Bonferroni correction for post hoc multiple comparisons regarding LCPLTAS in the three diagnostic groups

(I) 1 = single aMCI 2 = multiple aMCI 3 = healthy	(J) 1 = single aMCI 2 = multiple aMCI 3 = healthy	Mean difference (I–J)	SE	*P*-value	95% CI	
					Lower bound	Upper bound
1	2	69.5920*	4.66680	0.000	58.2306	80.9533
	3	−25.7658*	5.05640	0.000	−38.0756	−13.4559
2	1	−69.5920*	4.66680	0.000	−80.9533	−58.2306
	3	−95.3577*	4.94472	0.000	−107.3957	−83.3198
3	1	25.7658*	5.05640	0.000	13.4559	38.0756
	2	95.3577*	4.94472	0.000	83.3198	107.3957

The error term is mean square (error) = 423.575. aMCI, amnestic mild cognitive impairment; CI, confidence interval; LCPLTAS, Legal Capacity for Property Law Transactions Assessment Scale.
*The mean difference is significant at the 0.05 level.

Table 6. Bonferroni correction for post hoc multiple comparisons regarding LCPLTAS in the three VRF groups

(I) VRF	(J) VRF	Mean difference (I–J)	SE	*P*-value	95% CI	
					Lower bound	Upper bound
0	1	30.8930*	5.04648	0.000	18.6073	43.1787
	2	80.4853*	4.63144	0.000	69.2100	91.7605
1	0	−30.8930*	5.04648	0.000	−43.1787	−18.6073
	2	49.5922*	5.01950	0.000	37.3722	61.8123
2	0	−80.4853*	4.63144	0.000	−91.7605	−69.2100
	1	−49.5922*	5.01950	0.000	−61.8123	−37.3722

The error term is mean square (error) = 423.575. LCPLTAS, Legal Capacity for Property Law Transactions Assessment Scale; VRF, vascular risk factor.
*The mean difference is significant at the 0.05 level.

scores on financial capacity performance in aMCI. Correlations were run only in aMCI, as no VRFs were reported by HCs.

As can be seen in by the descriptive statistics (see Table 1), two-way ANOVA revealed a main effect for the diagnosis group F (1, 112) = 4.596, $P = 0.012$, effect size $\eta^2p = 0.080$, a main effect for VRFs F(1, 112) = 6.274, $P = 0.003$, but no interaction of diagnosis x VRFs F(1, 112) = 1.185, $P = 0.310$ regarding MMSE scores. Post hoc tests are presented in Tables 2 and 3.

Means and SDs for LCPLTAS among diagnostic groups and VRFs (see Table 4) being similar when two-way ANOVA is applied reveal a main effect for the diagnosis group F(1, 108) = 41.231, $P < 0.001$, effect size $\eta^2p = 0.449$, and a main effect for VRFs F (1, 108) = 5.470, $P = 0.006$, effect size $\eta^2p = 0.098$. It is of interest that no interaction of diagnosis x VRFs was found F(1, 108) = 0.427, $P = 0.654$ regarding LCPLTAS scores (Tables 5 and 6).

Discussion

Although the performance of patients with vascular dementia in overall cognitive functioning (as measured by MMSE) and financial capacity (as measured by LCPLTAS) are severely impaired, as shown in a previous study,[13] in this study the same is supported for aMCI of both subtypes as their scores are more than 2 SDs from the mean of HCs. In addition to that, patients with aMCI with a high vascular burden more frequently presented in the category of multiple-domain aMCI than in the category of single-domain aMCI.

Another novel finding is that participants with aMCI who were considered to have a high vascular risk profile if they had two or more VRFs had a worse financial capacity performance than those who were considered to have a low vascular risk profile if they had less than two VRFs. This was based on the threshold that was selected, because it represents the combined effect of risk factors that have been shown to impair cognition in the relevant literature.[26,27] Although a hypothesis was made that there would be a combined effects of factors (diagnosis of different types of aMCI and condition of VRFs) on the dependent measures (MMSE and LCPLTAS), the effect of one independent variable (type of aMCI diagnosis group) does not depend on the effect of the other independent variable (existence of VRFs).

These findings are of importance to clinicians as well as society since financial capacity assessment in old age has raised a number of still unanswered questions regarding individual differences and factors that may play a role in the development of somewhat different profiles of cognitive deficits.[28–31]

One of the major limitations of this study was the small sample size and, especially, the lack of participants with aMCI reporting zero VRFs in this research. This may be attributable to the particularly scrupulous examination of a wide range of VRFs that were included and recorded based on the previous body of research protocols.[22,26,27] Another potential limitation is the lack of longitudinal data on the same patients,[32,33] as well as the use of a binary assessment of the VRFs and diseases (presence/absence) rather than following a

continuous scale paradigm (based on blood pressure and/or blood glucose level), but the binary approach has already been established and used in previous studies of this kind.[22]

Disclosure statement

None.

Author contributions

V.G. designed the study, collected the data, and wrote the article. M.T. supervised the study.

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