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ORIGINAL ARTICLE

Increases in total cholesterol and low density lipoprotein associated with decreased cognitive performance in healthy elderly adults

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Abstract
The current study examined associations between blood lipid profiles and cognitive functioning using a healthy non-demented elderly sample. The sample comprised 196 healthy volunteers (male; 86: female 110) aged 60–75 years from the Australian Research Council Longevity Intervention (ARCLI) study cohort. Serum total cholesterol (T-C), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c) and triglycerides (TGL) were collected, and participants completed the Swinburne University Computerized Cognitive Assessment Battery (SUCCAB). In line with prediction, higher levels of T-C and LDL-c were found to be associated with impaired speeds of response in tasks assessing recognition memory, working memory and inhibitory processing. However, contrary to prediction both TGL and HDL-c were found to be unrelated to cognitive functioning in the current sample. It is suggested that frontal lobe function may be differentially sensitive to the effects of T-C and LDL-c accumulation during the aging process. Future data collection as part of the larger ARCLI intervention study will provide important follow-up data regarding the ability of the baseline blood lipid data to predict subsequent cognitive change.

Keywords Cognition · Ageing · Blood lipids · Cholesterol · Triglycerides

Introduction

Dyslipidemia, together with other vascular risk factors, have been found to be associated with an increased relative risk of dementia during the aging process (Kloppenborg et al. 2008). Mechanisms of action for these effects may include the effect of cholesterol on the degradation of the amyloid precursor protein (Burns and Duff 2002), as well the contribution of cholesterol to atherosclerosis in the arteries and microvasculature of the brain (Franciosi et al. 2009; Morley and Banks 2010). A number of studies have previously investigated associations between dyslipidemia and dementia risk, however the effect of increased cholesterol levels on cognitive decline in healthy aging more generally is yet to be properly established.

Van den Berg et al. (2009) conducted a systematic review to investigate the effect of vascular risk factors on cognitive functioning in elderly, non-demented, participants. Seven studies examined relationships between blood lipids and cognitive function. Two out of five longitudinal studies (De Frias et al. 2007; Komulainen et al. 2006) were found to have significant associations with one or more measures of dyslipidemia and worse cognitive function. In the study by Komulainen et al. (2006) low HDL-c was associated with increased risk of poor memory after 12 year follow-up, whilst in the study by de Frias et al. (2007) high triglyceride levels were associated with a greater 10 year decline in verbal knowledge. In contrast, in the studies by Teunissen et al. (2003) and Reitz et al. (2005), blood lipid levels were found to be unrelated to changes in cognitive function over 6 and 7 years, respectively, whilst in a study by Henderson et al. (2003) increases in T-C and LDL-c over an 8 year period were associated with *better* memory performance.

In relation to the two cross-sectional studies (Dik et al. 2007; Zhang et al. 2004) listed in the review by Van den Berg et al. (2009), only one of these studies (Dik et al. 2007) reported a significant association between dyslipidemia and worse cognitive function. In the study by Dik et al. (2007), which utilized a sample of 1183 participants aged 65–85 years, low HDL-c was found to be associated with impaired

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processing speed and fluid intelligence after controlling for age, sex and education, while triglyceride levels were not found to be associated with any of the cognitive measures. However, it is noteworthy that the sample included some participants with mild-moderate cognitive impairment, as evidenced by MMSE scores in the range of 16 to 30. In contrast, the study by Zhang et al. (2004), which utilized a sample of 4110 men aged 20–59 years, reported higher levels of serum T-C and non-HDL cholesterol to be associated with faster visuomotor speeds, as measured by a computerized simple reaction time test. Further, no association between T-C and cognitive function was found in the baseline data of Teunissen et al. (2003).

Additional studies, which were not included in the systematic review by Van den Berg et al. (2009), have also provided mixed findings. A prospective study by Ancelin et al. (2014) provided evidence to suggest that for elderly men a hypercholesterolemic pattern, consisting of high T-C, low HDL-c and high LDL-c was associated with a 25–50% increased risk of declines in psychomotor speed, executive abilities and verbal fluency over a 7 year period. Leritz et al. (2016) found that memory performance was negatively associated with triglyceride levels but positively associated with LDL-c, whilst executive function and language ability were not found to be associated with any of the serum cholesterol measures. In a more recent study by Lu et al. (2017) a quadratic relationship was found between T-C and cognitive performance, whereby males with either low or high T-C levels, rather than mid-range levels, performed worse on measures of executive function, attention and processing speed. However, other cross-sectional studies have reported better cognitive performance associated with higher levels of T-C (Elkana et al. 2018; Mielke et al. 2008) or LDL-c (Leritz et al. 2016), and a prospective study by Henderson et al. (2003) found increases in T-C and LDL-c over an 8-year period were associated with better memory performance.

In light of the previous inconsistencies reported in the literature, regarding the relationship between blood lipids and cognitive decline function, the aim of the current study was to investigate the relationship between total serum cholesterol (T-C), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), triglycerides (TGL) and cognitive function using a sensitive computerized cognitive battery in a sample of high-functioning healthy older adults without diabetes or dementia. It was hypothesised that higher T-C, LDL-c and TGL levels would be associated with decreased accuracy and slower reaction times in cognitive tasks, whereas it was also hypothesised that high HDL-c levels would be associated with improved accuracy and faster reaction times in cognitive tasks.

Methods

Participants

The sample comprised 196 healthy volunteers (Male; 86: Female 110) aged 60–75 years from the Australian Research Council Longevity Intervention (ARCLI) study cohort (Stough et al. 2012a). The data for this analysis was drawn from baseline data from the ARCLI study (a large intervention study aimed at examining the effects of two compounds on cognitive performance), whereby a complete case approach was used in relation to missing blood lipid or cognitive data.

Participant recruitment

Participants were recruited through radio, newspaper articles as well as poster and flyer distribution. Volunteers were excluded if they were taking cognitive enhancing supplements (e.g. *Ginkgo biloba*), were current smokers, had a history of drug and/or alcohol misuse or were currently taking prescribed antidepressant, anxiolytic or antipsychotic medication. Participants were eligible if they did not have a diagnosis of diabetes, dementia, neurological or psychiatric disorder or cardiovascular disease. Eligibility also included not having a recent history (defined as a period longer than 6 weeks, over the past 5 years), of a chronic or severe illness. Initial telephone screening was conducted by an experienced research assistant using participant self-reports. A second round of face-to-face interviewing was conducted to confirm eligibility according to the following screening measures: the Mini Mental State Examination (MMSE; Folstein et al. 1975) excluding those with a score of 23 or less which indicates cognitive impairment; and the Geriatric Depression Scale (GDS; Yesavage et al. 1982) excluding those with a score of 20 or more, which is indicative of depressive symptoms in the severe range. All participants provided written and informed consent, and the Swinburne University Human Research Ethics Committee approved the study. The ARCLI trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR12611000487910).

The Swinburne University computerised cognitive assessment battery (SUCCAB)

Cognitive function across a number of domains were also assessed using the SUCCAB, which is a computerized cognitive battery that was developed specifically for the detection of changes in cognition associated with aging (Pipingas et al. 2010). In the current study, sub-tests were administered in the following order: a simple recognition memory task (testing immediate memory of abstract pictures), a congruent colour-word stroop task, an incongruent colour-word stroop task, a spatial working memory task (testing working memory of spatial locations), a contextual recognition memory task (testing the learning of associations between objects and their location) and a delayed recognition memory task (testing the recall of previously presented abstract pictures). Further details regarding these computerized tasks have been described in Pipingas et al. (2010). The outcome measures for each tasks were response time (in milliseconds) and accuracy (percentage of correct responses) for each of the memory tasks.

Screening and clinical scales

Mini-mental state examination (MMSE) The Mini-Mental State Examination (MMSE; Folstein et al. 1975) is a brief 30-point test that is commonly used to screen for dementia. The MMSE evaluates six areas of cognitive function: orientation, attention, immediate recall, short-term recall, language, and the ability to follow simple verbal and written commands. Scores ≥24 points indicate normal cognition, whereas scores below this level indicate some level of cognitive impairment (Folstein et al. 1975).

Wechsler abbreviated scale of intelligence (WASI) Two tests from the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler 1999) were administered in order to provide an estimate of the full scale intelligence quotient (IQ). The vocabulary and matrix reasoning subtests of the WASI were administered to all participants. The vocabulary subtest is a 42-item task, which requires the participant to orally define words that are presented visually and orally. The matrix reasoning subtest involves the presentation of a series of 35 incomplete grid patterns, which the participant is asked to complete by selecting the correct pattern from five possible choices. The WASI is a reliable and valid measure of intelligence for use in research settings (Canivez et al. 2009).

Geriatric depression scale (GDS) The GDS (Yesavage et al. 1982) is a basic screening measure for depressive symptom severity which is suitable for use in elderly populations. The GDS sums 30 questions each of which are answered "yes" or "no". A total score of 0–9 is considered normal, a score of 10–19 indicates mild depressive symptoms and a score of 20–30 indicates severe depressive symptoms.

Blood sampling For each participant, 8.5 ml of blood was collected via venepuncture into a serum-separator tube following an overnight fast of ≥12 h. The samples were centrifuged for 10 min at 4000 rpm, then stored at 4 °C before being sent to a commercial laboratory in Melbourne, Victoria for analysis (Clinicallabs Pathology). Serum concentrations of total cholesterol (T-C), triglycerides (TGL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were measured using the ADVIA system (Siemens, USA) according to standard enzymatic methods (Appleton et al. 2007).

Procedure Participants attended Swinburne University of Technology in Melbourne for two sessions with the visits being up to one week apart. Eligible participants could attend during the morning or afternoon with the allocated time of day remaining consistent, minimizing confounding effects of fatigue and diurnal variation on cognitive and blood parameters. Morning participants attended after fasting overnight while afternoon participants were able to consume a light breakfast and lunch. At the beginning of the first visit, participants provided written and informed consent prior to engaging in any screening questionnaires or undergoing blood pressure measurements or cognitive test batteries. Participants were screened for depressive symptoms and any possible memory impairments using the GDS and the MMSE, respectively. General cognitive ability (IQ) was assessed using the WASI. General demographic information was also collected at the time of the first visit, including age, gender, height, weight, body mass index (BMI) and total years of education (including primary school). Blood pressure measurements were assessed at the second visit, prior to participants completing the computerized cognitive tasks.

Statistical analysis All analyses were conducted using IBM SPSS Statistics Version 25. Confirmatory factor analysis (CFA) was conducted in IBM SPSS AMOS 25 Graphics. Initial exploratory correlations were conducted in order to test for patterns of association between demographic variables and both blood lipid and SUCCAB cognitive outcome measures. Age, body mass index (BMI), years of education and intelligence (WASI) were found to form significant correlations ($p < .05$) and for this reason were included as covariates in all subsequent analyses. Participants were then divided into high and low blood lipid groups on the basis of median splits for T-C, LDL-cholesterol, HDL-cholesterol and Triglycerides.

For SUCCAB simple recognition memory, spatial working memory, delayed recognition memory and the stroop task repeated measures analysis of covariance (ANCOVA) was used to test for the effects of blood lipid concentration on cognitive performance. Separate analyses were conducted for accuracy (% correct) and reaction time (*ms*) for each of T-C, LDL-cholesterol, HDL-cholesterol and triglyceride groups. In each analysis, blood lipid group (high, low) and gender (male, female) were included as between-subject variables, and stimulus type (original/novel for the memory tasks, and congruent/incongruent for the stroop task) was included as the within-subject variable. In the case of significant main effects or interactions ($p < .05$), follow-up pairwise comparisons were conducted in order to test for the direction of the difference. For SUCCAB contextual recognition memory univariate ANCOVA was used to test for the effect of blood lipid concentration on cognitive performance using blood lipid group (high, low) and gender (male, female) as between-subject variables.

Results

Means, medians and standard deviations for demographic, screening and blood lipid measures are displayed in Table 1. Means and standard deviations of means for SUCCAB tests according to blood lipid groupings (T-C, LDL-cholesterol, HDL-cholesterol and triglycerides) are displayed in Table 2.

Simple recognition memory

Reaction time A significant gender × stimulus type interaction was observed (F(1,190) = 4.593, *p* = .033, partial η^2 = .024), whereby males were significantly slower than females when responding to original stimuli (males: M = 993.27, SE = 15.05, females: M = 940.52, SE = 13.28, *p* = .010). A significant main effect was observed for T-C (F(1,188) = 4.146, *p* = .043, partial η^2 = .022), whereby participants in the high cholesterol group had slower reaction times than participants in the low cholesterol group (high cholesterol: M = 1016.17, SE = 12.01, low cholesterol: M = 982.22, SE = 11.42, p = .043).

Accuracy A significant T-C × stimulus type interaction was observed (F(1,188) = 5.118, *p* = .025, partial η^2 = .027), whereby there was a trend (*p* < .10) towards participants in the high cholesterol group being more accurate than participants in the low cholesterol group for original stimuli (high cholesterol: M = 63.77%, SE = 1.98, low cholesterol: M = 58.71%, SE = 1.85, *p* = .063).

Stroop task

Reaction time Significant main effects were observed for T-C (F(1,188) = 8.310, *p* = .004, partial η^2 = .042) and low density lipoprotein (F(1,188) = 5.761, *p* = .017, partial η^2 = .030), whereby participants in the high cholesterol group had slower reaction times than participants in the low cholesterol group (high cholesterol: M = 896.14, SE = 11.02, low cholesterol: M = 852.06, SE = 10.47, p = .004) and participants in the high LDL group had slower reaction times than participants in the low LDL group (high LDL: M = 885.72, SE = 10.60, low LDL: M = 848.96, SE = 10.94, p = .017). A significant gender × T-C interaction was observed (F(1,188) = 13.472, *p* < .001, partial η^2 = .067) together with a significant gender × low density lipoprotein interaction (F(1,188) = 4.402, *p* = .037, partial η^2 = .023). Males in the high cholesterol group had significantly slower reaction times than males in the low cholesterol group (high cholesterol: M = 934.42, SE = 17.86, low cholesterol: M = 834.47, SE = 14.37, p < .001), and males in the high LDL group had significantly slower reaction times than males in the low LDL group (high LDL: M = 906.68, SE = 15.89, low LDL: M = 837.87, SE = 16.61, *p* = .003). *Accuracy:* No significant main effects or interactions were found for stroop accuracy.

Contextual recognition memory

Reaction time Significant main effects were observed for T-C (F(1,188) = 5.395, *p* = .021, partial η^2 = .028) and low density lipoprotein (F(1,188) = 5.207, *p* = .024, partial η^2 = .027). Participants in the high cholesterol group performed significantly slower than participants in the low cholesterol group (high cholesterol: M = 1088.66, SE = 13.45, low cholesterol: M = 1045.30, SE = 12.78, p = .021). Participants in the high LDL group performed significantly slower than participants in the low LDL group (high LDL: M = 1083.94, SE = 12.61, low LDL: M = 1042.36, SE = 13.02, p = .024). *Accuracy:* No

Table 1 Means, medians and standard deviations of demographic, screening and blood lipid measures

	Males (*n* = 86)			Females (*n* = 110)			Overall (*n* = 196)		
	M	median	(SD)	M	median	(SD)	M	median	(SD)
Demographic and screening measures									
Age (years)	66.37	66.00	(3.80)	65.65	65.00	(4.09)	65.96	66.00	(3.97)
Body Mass Index	26.33	25.85	(3.90)	25.47	24.63	(4.57)	25.84	25.39	(4.30)
Education (total years)	16.57	17.00	(3.62)	15.79	16.00	(4.44)	16.13	16.00	(4.11)
Intelligence†	119.51	121.00	(10.60)	119.16	120.00	(11.86)	119.32	121.00	(11.29)
Mini Mental Status Examination	28.31	29.00	(1.41)	28.94	29.00	(1.14)	28.66	29.00	(1.30)
Geriatric Depression Scale	3.70	3.00	(3.75)	3.77	3.00	(3.56)	3.74	3.00	(3.63)
Blood Lipid measures									
Total cholesterol (mmol/L)	5.25	5.30	(.99)	5.67	5.70	(.79)	5.49	5.45	(.91)
Low density lipoprotein cholesterol (mmol/L)	3.18	3.30	(.84)	3.29	3.30	(.73)	3.24	3.30	(.78)
High density lipoprotein cholesterol (mmol/L)	1.46	1.40	(.41)	1.91	1.90	(.49)	1.71	1.60	(.51)
Triglycerides (mmol/L)	1.39	1.20	(.80)	1.05	.90	(.51)	1.20	1.00	(.67)

† Fullscale intelligence quotient obtained using the Wechsler Abbreviated Scale of Intelligence (WASI)

Table 2 Means and Standard deviations of SUCCAB outcome variables, by blood lipid groupings

	Total cholesterol		Low Density Lipoprotein		High Density Lipoprotein		Triglycerides	
	Low M (SD)	High M (SD)	Low M (SD)	High M (SD)	Low M (SD)	High M (SD)	Low M (SD)	High M (SD)
Simple Recognition Memory								
Accuracy (%)	60.07 (15.61)	62.11 (15.64)	60.74 (16.02)	61.42 (15.30)	60.39 (15.72)	61.62 (15.59)	63.30 (14.44)	59.21 (16.39)
RT (ms)	983.10 (108.47)	1006.09 (118.15)	982.00 (112.68)	1006.45 (113.95)	1004.75 (111.32)	986.82 (115.40)	989.92 (110.27)	998.57 (116.91)
Stroop Congruent								
Accuracy (%)	96.12 (5.48)	96.84 (5.03)	96.53 (5.22)	96.44 (5.32)	96.06 (5.78)	96.80 (4.83)	97.28 (3.63)	95.80 (6.26)
RT (ms)	790.22 (108.95)	817.12 (120.10)	786.89 (112.46)	819.45 (115.99)	800.52 (120.74)	806.08 (111.19)	808.46 (112.63)	799.60 (117.65)
Stroop Incongruent								
Accuracy (%)	89.80 (19.09)	91.35 (11.67)	91.03 (17.87)	90.15 (13.65)	89.68 (16.81)	91.26 (15.03)	90.50 (15.37)	90.64 (16.23)
RT (ms)	917.69 (128.77)	943.50 (127.93)	913.39 (124.01)	946.79 (131.47)	937.44 (137.94)	925.36 (121.48)	934.96 (122.47)	926.90 (134.18)
Contextual Recognition Memory								
Accuracy (%)	68.27 (18.05)	68.72 (19.09)	68.95 (17.40)	68.07 (19.62)	70.12 (16.60)	67.25 (19.87)	70.56 (16.12)	66.75 (20.27)
RT (ms)	1046.80 (129.28)	1078.51 (138.83)	1042.54 (126.04)	1081.57 (140.44)	1052.87 (133.81)	1070.15 (135.57)	1065.82 (130.85)	1059.97 (138.52)
Spatial Working Memory								
Accuracy (%)	73.56 (13.63)	70.77 (14.61)	73.20 (13.55)	71.20 (14.71)	75.67 (12.95)	69.48 (14.51)	72.26 (15.18)	72.09 (13.30)
RT (ms)	966.19 (123.37)	1019.22 (125.18)	971.74 (128.01)	1012.43 (122.99)	969.64 (128.48)	1010.37 (123.12)	991.17 (116.77)	994.01 (135.23)
Delayed Recognition Memory								
Accuracy (%)	70.45 (10.40)	70.02 (11.53)	71.06 (10.15)	69.46 (11.66)	71.06 (9.12)	69.60 (12.18)	70.13 (11.19)	70.32 (10.80)
RT (ms)	1003.22 (113.75)	1011.87 (103.58)	993.34 (109.68)	1020.90 (106.38)	1017.08 (110.32)	1000.24 (107.18)	998.96 (112.97)	1014.83 (104.71)

significant main effects or interactions were found for contextual recognition memory accuracy.

Spatial working memory performance

Reaction time For Spatial working memory reaction time, significant main effects were found for T-C ($F(1,188) = 12.107$, $p = .001$, partial $\eta^2 = .061$) and low density lipoprotein ($F(1,188) = 6.410$, $p = .012$, partial $\eta^2 = .033$). Participants in the high cholesterol group performed significantly slower than participants in the low cholesterol group (high cholesterol: M = 1027.32, SE = 12.80, low cholesterol: M = 965.50, SE = 12.16, p = .001). Participants in the high LDL group performing significantly slower than participants in the low LDL group (high LDL: M = 1014.60, SE = 12.21, low LDL: M = 969.96, SE = 12.60, p = .012). *Accuracy:* No significant main effects or interactions were found for spatial working memory accuracy.

Delayed recognition memory

Reaction time A significant main effect for gender was observed ($F(1,190) = 4.346$, $p = .038$, partial $\eta^2 = .022$), with males performing significantly slower than females (males: M = 1031.49, SE = 11.89, females: M = 998.15, SE = 10.49, p = .038). A significant main effect for low density lipoprotein was also observed ($F(1,188) = 4.583$, $p = .034$, partial $\eta^2 = .024$), whereby participants in the high LDL group performed significantly slower than participants in the low LDL group (high LDL: M = 1031.18, SE = 10.92, low LDL: M = 997.40, SE = 11.27, p = .034).

Accuracy A significant T-C × stimulus type interaction was observed ($F(1,188) = 4.274$, $p = .040$, partial $\eta^2 = .022$) whereby in the high cholesterol group accuracy was significantly better for original stimuli compared to novel stimuli (original stimuli: M = 74.38%, SE = 1.53, novel stimuli: M = 65.06%, SE = 1.66, $p < .001$).

Discussion

Higher levels of serum T-C were found to be associated with slowed speed of response across multiple cognitive domains, including simple recognition memory, inhibitory processing (stroop), contextual recognition memory and spatial working memory. Similarly, higher levels of LDL-c were also found to be associated with a decreased speed of response for inhibitory processing (stroop), contextual recognition memory, spatial working memory and delayed recognition memory. HDL-c and triglycerides were found to be unrelated to the cognitive outcome measures included in the battery, whilst accuracy in the cognitive tasks was unrelated to any of the blood lipid measures.

The current findings for T-C and LDL-c are consistent with the prospective study by Ancelin et al. (2014) whereby a hypercholesterolemic pattern in late-life men, consisting of high T-C, low HDL-c and high LDL-c was associated with a 25–50% increased risk of declines in psychomotor speed, executive abilities and verbal fluency over a 7 year period. The current findings are also partially consistent with the study by Lu et al. (2017) whereby males with either low or high T-C levels, rather than mid-range levels, performed worse on measures of executive function, attention and processing speed. However, these findings are in contrast to previous cross-sectional studies which have reported better cognitive performance associated with higher levels of T-C (Elkana et al. 2018; Mielke et al. 2008; Zhang et al. 2004) or LDL-c (Leritz et al. 2016), and the prospective study by Henderson et al. (2003) whereby increases in T-C and LDL-c over an 8-year period were found to be associated with better memory performance. Similarly the current findings diverge from previous studies which observed no relationship between T-C, LDL-c and cognitive outcome measures (Dik et al. 2007; Reitz et al. 2005; Teunissen et al. 2003).

The finding of no associations between HDL-c and cognitive performance was consistent with some previous studies (Leritz et al. 2016; Reitz et al. 2005; Teunissen et al. 2003). However, these findings were in contrast to a number of studies which reported impaired cognitive performance associated with low HDL-c (Dik et al. 2007; Mielke et al. 2008) or increased risk of declines associated with low HDL-c (Ancelin et al. 2014; Komulainen et al. 2006). Similarly, the current findings are in contrast to the study by Lu et al. (2017) where women with mid-range HDL-c performed better than those with low or high HDL-c across a number of domains. The finding of no association between TGL and cognitive performance was also consistent with a large number of previous studies (Ancelin et al. 2014; Dik et al. 2007; Henderson et al. 2003; Komulainen et al. 2006; Reitz et al. 2005; Teunissen et al. 2003), yet in contrast to the findings of Leritz et al. (2016) and Frias et al. (De Frias et al. 2007) where higher TGL levels were associated with worse memory function and a greater subsequent decline in verbal knowledge, respectively.

Due to the large degree of heterogeneity in both sample characteristics and cognitive outcome measures used across previous studies, it is difficult to clearly identify reasons for the strong pattern of association between T-C, LDL-c and cognitive impairment observed in the current study, and the lack of association found for HDL-c and TGL. However, what can be observed from the current demographics (see Table 1) is that the sample consisted of late middle-age participants (M = 65.96 years, SD = 3.97), that were well educated (M = 16.13, SD = 4.11), with above average intelligence (M =

119.32, SD = 11.29), and no evidence of either depression (GDS; M = 3.74, 3.63) or cognitive impairment (MMSE scores ≥24 points). Similarly, by observing the lipid profiles of participants for the sample as a whole it can be seen that the participants are on average in the normal range. According to the third report of the National Cholesterol Education Expert Panel (NCEP Expert Panel 2001) the T-C median of 5.45 mmol/L is within the 'borderline' range (5.2 – 6.2 mmol/L), the LDL-c median of 3.30 mmol/L is at the upper limit of the 'good' range (2.6 – 3.3 mmol/L), the HDL-c median of 1.60 mmol/L is within the 'good' range (>1.55 mmol/L), and the TGL median of 1.0 mmol/L is also within the 'desirable' range (< 1.7 mmol/L). For these reasons, it is most accurate to interpret the current relationships between T-C, LDL-c and cognitive function within the context of healthy late-middle age individuals who do not have clinically elevated blood lipid profiles. Another important factor which differentiates the current study from many previous studies is that it utilized a computerized (speeded) cognitive battery which measured both memory recall as well as inhibitory processes and working memory function. In consideration of the fact that it was the reaction times, rather than the accuracies, that were found to form significant associations with the blood lipid measures it could be argued that previous studies which do not measure speed-of-response (i.e. utilize only global measures such as the MMSE, or paper-and-pencil tasks without millisecond precision), may have failed to capture these relationsihps.

In regard to interpreting the possible effect of T-C and LDL-c on cognitive abilities, it is interesting to note that both the spatial working memory and stroop (inhibitory processing) task rely predominantly on frontal lobe functioning, which suggests that blood lipids may be detrimentally impacting function in this area of the brain, a region which has been found to be particularly vulnerable to structural changes during the aging process (Hedden and Gabrieli 2004). However, it is noteworthy that higher T-C and LDL-c levels were also associated with declines in performance for simple recognition, learning of contextual associations and delayed recognition memory, indicating that the medial temporal lobes may also be effected early in the aging process by accumulation of blood lipids. A potential common mechanism by which elevated T-C and LDL-c may impact brain functioning within these disparate regions is via atherosclerosis in the arteries and microvasculature providing blood to this region (Franciosi et al. 2009; Morley and Banks 2010).

An important limitations of the current study was that it was only cross sectional in nature, and hence there needs to be caution in inferring mechanisms of causality. However, longitudinal data is to be obtained over a 12-month period for participants enrolled in the intervention phase of the ARCLI study (Stough et al. 2012b). With this data it will be possible to compare changes over time on both blood lipid and cognitive data, and also to test how baseline blood lipid profiles predict subsequent changes in cognition of the subsequent 12-month period.

In summary, the current study examined associations between blood lipid profiles and cognitive functioning using a healthy non-demented elderly sample. In line with prediction, higher levels of T-C and LDL-c were found to be associated with impaired speeds of response in tasks assessing recognition memory, working memory and inhibitory processing. However, contrary to prediction both TGL and HDL-L were found to be unrelated to cognitive functioning in the current sample. A number of these tasks rely on intact frontal lobe function, which suggests that these structures may be differentially sensitive to the effects of T-C and LDL-c accumulation during the aging process. Future data collection as part of the larger ARCLI intervention study will provide important follow-up data regarding the ability of the baseline blood lipid data to predict subsequent cognitive change.

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Compliance with ethical standards

Conflict of interest The authors have no actual or potential conflict of interests to declare with respect to the research, authorship, and/or publication of this article.

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