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Cognitive Performance Is Correlated with Serum Lipoproteins

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ABSTRACT

Introduction: Emerging evidence suggests that lipoproteins levels are associated with cognitive health. This study examines the relationship between lipoprotein levels and cognitive performance in middle-aged and young adults. It addresses the impact of abnormal lipid levels and hypercholesterolemia on cognitive impairment .

Methods: We performed a cross-sectional study involving 123 healthy security guards aging 20- 60 years old. Lipid profiles included total cholesterol (TC), low-density lipoprotein, high-density lipoprotein (HDL) and triglyceride (TG) levels were measured in serum. EEG recording was used to obtain the cognitive indicators of attention, memory, salience, language, mood and executive function. Spearman correlation analysis was used to determine the correlation between lipoproteins and cognitive indices.

Results: A significant relationship with executive function was found for TC (r = -0.2944, p = 0.0202) and LDL (r = -0.3687, p = 0.0032). Additionally, a significant relationship was found between attention and serum HDL levels (r = -0.1987, p = 0.0296). In middle-aged security guards, there was a significant correlation between attention and TC (r = -0.4338, p = 0.0187) and LDL (r = -0.3909, p = 0.0360). Also, there was a significant correlation between executive function and TC (r = -0.5475, p = 0.0368) as well as LDL (r = -0.6709, p = 0.0077).

Conclusion: Our findings suggest that executive function and attention are key cognitive indices significantly linked to lipoproteins. In the middle-age group, higher TC and LDL levels correlated with lower cognitive scores compared to the general population, indicating a potential role of lipoprotein factors in cognition.

Keywords: cholesterol, lipoproteins, cognitive performance, attention, executive function.

INTRODUCTION

Cognitive impairment is characterized by deterioration in memory, thinking, attention, language, and executive function. Cognitive impairment may affect a person's ability to perform daily activities and cause social and economic burdens (1, 2). Of these, abnormal lipid levels and hypercholesterolemia are emerging as important modifiable risk factors for CI and other psychiatric conditions (3-5). researchers believe that the relationship between lipoproteins and cognitive impairment is age-dependent, and mid-life hyperlipidemia is a risk factor for developing dementia or cognitive impairment at a later age

(6). Thus, Serum lipid levels are crucial factors associated with individual cognition (7).

Cognitive abilities are widely recognized as important predictors of job performance, but there is ongoing debate about the relative importance of general versus specific cognitive abilities in this context. Additionally, the role of cognitive abilities in complex occupations is not fully understood. The ongoing controversy underscores the need for further research to better understand the relationship between cognitive abilities and job performance (8-10). In our study, we conducted cognitive evaluations of security guards, analyzing six key indicators essential for their job performance: memory, attention, salience, executive function, language skills, and mood regulation. Proficiency in these specific cognitive abilities is crucial for men in security guard roles, as they are essential for recognizing threats, staying alert, responding to emergencies, making quick decisions, effective communication, and maintaining composure in high-pressure situations. The proper performance of these components is vital for their job and holds significance for recruitment and organizational cooperation. This research aims to shed light on the specific cognitive abilities that are most influential in the performance of security guards, ultimately contributing to a better understanding of the broader relationship between cognitive abilities and job performance in complex occupations.

Numerous cross-sectional and longitudinal studies have demonstrated that higher total cholesterol (11-14) and low-density lipoprotein (LDL) cholesterol levels (15-17) are linked to poorer cognitive performance, while higher high-density lipoprotein (HDL) cholesterol levels (15, 18) are associated with better maintenance of cognitive function. However, the relationship between triglycerides and cognitive indicators has yielded conflicting results, with some studies showing a positive relationship (19), some showing an inverse relationship (20, 21) , and others finding no relationship at all (22, 23). It's worth noting that the measures of cognitive functioning and the specific tasks used varied across these studies. Additionally, sex-specific brain network mechanisms and sex steroid hormones have been suggested to influence both serum lipid levels and cognitive performance, but the role of these factors remains unclear (7, 24).

Several possible mechanisms through which these factors influence cognitive function need to be clarified in order to fully understand their impact. The brain requires a constant blood supply, receiving about 20% of the body's total blood flow to provide oxygen and glucose essential for energy production and maintaining neuronal activity (25). The changes in regional blood flow associated with task performance are often no more than 5% of the resting blood flow of the brain (25). Any increase or disturbance in the levels of factors in the blood can have a significant impact on the brain due to its high blood flow. In humans, the brain has the second-highest lipid content after adipose tissue, accounting for 50% of its dry weight (26). High lipid content plays a crucial role in the brain, because lipids provide structural integrity and modulate the fluidity of brain neuronal cells. Lipid dysregulation has been associated with the etiology and progression of neurodegeneration and other neurological pathologies (27, 28). Increasing levels of Apo A-I/plasma HDL induce the formation of Apo J complexes, which affect the blood-brain barrier transport, maintaining intact brain cell function (29). Hypertriglyceridemia impedes the transport of leptin, a pleiotropic hormone that influences neuronal survival, learning, and memory, across the blood-brain barrier (30). It also changes cerebral blood by increasing blood viscosity and lowers cognitive function by causing arteriosclerosis (31). Vascular risk factors like dyslipidemia may adversely affect brain function،Elevated TC and LDL may impact brain functioning via atherosclerosis in the arteries and microvasculature providing blood to these regions (32, 33).Only HDL appear to traverse the blood-brain barrier (BBB); thus, lipoproteins found in the brain must be produced within the central nervous system. In the hippocampus and other brain regions, lipoproteins help to regulate neurobehavioral functions through lipoprotein receptor-mediated processes (34) and can lead to altered brain morphology (35).

Although reports have established a connection between blood lipid levels and cognitive health, the specific impact of lipoprotein levels on cognitive functioning in various tasks remains unclear. Furthermore, the relationship between lipoproteins and cognitive indices has primarily been studied in middle-aged and elderly adults, overlooking the younger population. This study aims to investigate the association between lipoprotein levels and cognitive performance in both middle-aged and young adults, focusing on six specific cognitive characteristics. By doing so, it seeks to provide a more comprehensive understanding of this relationship across different age groups.

MATERIALS AND METHODS

Participants

This cross-sectional study was conducted among 148 men security guards aged 20-60 from an Iranian population. However, 25 individuals were excluded due to factors such as a history of neurological disorders, substance abuse or dependence, medications affecting EEG recording, and the presence of metal implants or devices, as determined through questionnaire and interview responses. As a result, our final analysis included 123 healthy subjects who were in good physical and mental condition.

Data collection

Data collection was carried out in 2022-2023. At 7 am to 1 pm, blood samples were collected from the participants. Following breakfast, interviews, and filling out the questionnaire, qualitative electroencephalography was conducted. Information obtained through interviews and questionnaires revealed that participants with cognitive impairment, psychiatric conditions, neurological disorders, recent strokes, recent major surgeries, epilepsy, brain injury, or current use of medications affecting EEG signals were excluded from the study.

Lipid measurement

Overnight fasting blood samples were collected at 8 am during the medical check, and plasma lipids, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), were immediately measured. For a more detailed evaluation, different levels of plasma lipoproteins were classified into three classes, and lipid measurements were categorized into optimal, intermediate, and high based on specific ranges (36). For TC, the optimal range was less than 200 mg/dL, intermediate fell between 200-239 mg/dL, and high exceeded 239 mg/dL. LDL levels were considered optimal if they were less than 130 mg/dL, intermediate between 130-159 mg/dL, and high if they exceeded 159 mg/dL. HDL levels were optimal if they were greater than 60 mg/dL, intermediate between 40-60 mg/dL, and high if they were less than 40 mg/dL. TG levels were categorized as optimal if they were less than 150 mg/dL, intermediate between 150-159 mg/dL, and high if they exceeded 159 mg/dL.

Cognitive assessment

The qEEG data were recorded using the Mitsar M201 (Russia) device with an Electro-Cap containing 19 channels. The electrode montage was based on the 10-20 universal system. The recordings were conducted with participants in a resting state and with their eyes closed. These qEEG measurements were consistently performed at the same location and time of day (morning to noon), with each session lasting approximately seven minutes. During the recording phase, WinEEG software was utilized, while Neuroguide software was employed for signal preprocessing. The sampling frequency was set at 250Hz, and impedances were maintained below 20 kΩ. Following the initial recording, an offline filter was applied, and the Independent Component Analysis (ICA) algorithm was utilized to identify and separate various independent sources. During the artifact rejection phase, ICA components related to eye movement, heart activity, and other sources of noise were removed. Subsequently, total scores for each cognitive function, including memory, attention, salience, language skills, mood, and executive function were calculated based on the processed qEEG data.

Statistical analysis

Spearman correlation analysis was chosen due to the non-parametric nature of the data distribution. Before conducting the analysis, the normality of the data was assessed using Shapiro-Wilk. The significance level was set at $\alpha = 0.05$ for all statistical tests. The correlations between total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride levels with cognitive scores for memory, attention, salience, language skills, mood, and executive function were evaluated using GraphPad Prism software version 9 (GraphPad Software, San Diego, CA). If a p-value is less than 0.05, it is flagged with one star (*). If a p-value is less than 0.01, it is flagged with 2 stars (**). P-value, p-value summary, and correlation coefficient are reported in table 4 to provide a comprehensive understanding of the statistical significance and strength of the relationships observed in the data analysis. Additionally, correlations were examined between optimal, intermediate, and high levels of lipoproteins and the cognitive scores. These analyses were performed separately for young adults and middle-aged adults to account for potential age-related differences in the relationships between lipid profiles and cognitive functions.

Ethical approval for research study

Before initiating the study, ethical approval was obtained from the Ethics Committee/Institutional Review Board under the ethical code (IR.AJAUMS.REC.1400.165) to ensure adherence to ethical standards and guidelines.

RESULTS

Age, BMI, and lipoprotein profiles in young and middle-aged adults

The data presented in Table 1 and Table 2 includes the age, BMI, and lipoprotein profiles (TC, LDL, HDL, and triglycerides) categorized as optimal, intermediate, and high. The study also involved separate examinations of young adults and middle-aged adult.

Assessment of cognitive indices in general population, young, and middle-aged adults

Table 3 indicates the scores of cognitive indices, including memory, attention, salience, executive function, language ability, and mood, obtained by the Neuroguide software for the general population and young and middle-aged adults.

Correlation analysis of lipid levels with cognitive indicators in different age groups

In Table 4, the correlation analysis investigated the associations between total cholesterol (TC), LDL cholesterol, HDL cholesterol, triglyceride levels, and various cognitive indicators, focusing on significant correlations ($p < 0.05$). Notably, a significant negative correlation was identified between executive functions and TC ($r = -0.2944$, $p = 0.0202$), as well as between executive functions and LDL cholesterol ($r = -0.3687$, $p = 0.0032$), suggesting a potential impact on cognitive performance. Additionally, attention exhibited a significant negative correlation with HDL cholesterol ($r = -0.1987$, $p = 0.0296$).

Table 1. Age, BMI in young and middle-aged adults

CHARACTERISTICS		Mean ± SD	Minimum	Maximum
Age (years)		36.54 ± 7.339	22	60
Young Adult No. (%) of subjects	93 (76)	33.31 ± 4.240	22	41
Middle-aged adult No. (%) of subjects	30 (24)	46.53 ± 5.728	40	60
BMI (kg/m²)		27.58 ± 5.549	15.70	51
Young Adult No. (%) of subjects	93 (76)	26.88 ± 5.235	15.70	46.00
Middle-aged adult No. (%) of subjects	30 (24)	29.63 ± 6.014	19.00	51.00

Table 2. Lipoprotein profiles in young and middle-aged adults

SERUM LIPID PARAMETERS		Mean ± SD	Range	Minimum	Maximum
TC (mg/dl)		182.2 ± 33.52	177	107	284
Optimal No. (%) of subjects	88 (72)	165.2 ± 19.90	91.00	107.0	198.0
Intermediate No. (%) of subjects	31 (25)	219.8 ± 13.51	59.00	200.0	259.0
High No. (%) of subjects	4 (3)	263.8 ± 20.37	44.00	240.0	284.0
Young Adult No. (%) of subjects	93 (76)	179.7 ± 31.04	152.0	107.0	259.0
Middle-aged adult No. (%) of subjects	30 (24)	189.6 ± 39.94	152.0	132.0	284.0
LDL (mg/dl)		110.3 ± 28.17	156	30	186
Optimal No. (%) of subjects	92 (75)	97.36 ± 17.42	99.00	30.00	129.0
Intermediate No. (%) of subjects	24 (20)	141.8 ± 9.085	28.00	130.0	158.0
High No. (%) of subjects	7 (5)	172.9 ± 11.23	27.00	159.0	186.0
Young Adult No. (%) of subjects	93 (76)	108.4 ± 27.48	156.0	30.00	186.0
Middle-aged adult No. (%) of subjects	30 (24)	116.2 ± 29.93	114.0	70.00	184.0
HDL (mg/dl)		42.30 ± 8.100	46	21	67
Optimal No. (%) of subjects	2 (2)	63.50 ± 4.950	7.000	60.00	67.00
Intermediate No. (%) of subjects	76 (62)	46.50 ± 4.981	19.00	40.00	59.00
High No. (%) of subjects	45 (36)	34.27 ± 4.707	18.00	21.00	39.00
Young Adult No. (%) of subjects	93 (76)	42.05 ± 7.830	42.00	25.00	67.00
Middle-aged adult No. (%) of subjects	30 (24)	43.07 ± 8.982	38.00	21.00	59.00
TG (mg/dl)		148.2 ± 54.55	246	53	299
Optimal No. (%) of subjects	69 (56)	109.0 ± 23.65	96.00	53.00	149.0
Intermediate No. (%) of subjects	33 (27)	172.2 ± 14.58	46.00	150.0	196.0
High No. (%) of subjects	21 (17)	239.1 ± 31.39	100.0	199.0	299.0
Young Adult No. (%) of subjects	93 (76)	146.9 ± 55.22	240.0	59.00	299.0
Middle-aged adult No. (%) of subjects	30 (24)	152.1 ± 53.14	213.0	53.00	266.0

Table 3. Cognitive indices in general population, young, and middle-aged adults

Cognitive indices (0-100)	Mean ± SD	Cognitive indices (0-100)	Mean ± SD
Memory	31.62 ± 31.97	**Executive Function**	31.65 ± 30.96
Young Adult No. (%) of subjects	30.78 ± 32.28	**Young Adult** No. (%) of subjects	32.66 ± 30.22
Middle-aged adult No. (%) of subjects	34.17 ± 31.39	**Middle-aged adult** No. (%) of subjects	28.47 ± 34.08
Attention	44.08 ± 27.86	**Language**	36.98 ± 30.64
Young Adult No. (%) of subjects	46.62 ± 29.06	**Young Adult** No. (%) of subjects	38.11 ± 30.62
Middle-aged adult No. (%) of subjects	36.10 ± 22.30	**Middle-aged adult** No. (%) of subjects	33.47 ± 31.49
Salience	44.10 ± 34.64	**Mood**	57.38 ± 32.52
Young Adult No. (%) of subjects	42.30 ± 36.67	**Young Adult** No. (%) of subjects	57.36 ± 33.72
Middle-aged adult No. (%) of subjects	49.73 ± 27.67	**Middle-aged adult** No. (%) of subjects	57.43 ± 29.11

Furthermore, in the middle-aged adult group, attention demonstrated significant negative correlations with both TC (r = -0.4338, p = 0.0187) and LDL cholesterol (r = -0.3909, p = 0.0360). Similarly, executive function showed significant negative correlations with TC (r = -

Table 4. Significant correlation pairs between lipoproteins and cognitive indices across general population, young adults, and middle-age adults

Significant Correlations	P value	P value Summary	Correlation Coefficient
All Participants			
Executive Function∞ TC	0.0202	*	-0.2944
Executive Function∞ LDL	0.0032	**	-0.3687
Attention ∞ HDL	0.0296	*	-0.1987
Executive Function ∞ Optimal LDL	0.0039	**	-0.4214
Attention ∞ Intermediate HDL	0.0028	**	-0.3449
Salience ∞ Intermediate TG	0.0119	*	-0.5503
Mood ∞ Intermediate TG	0.0112	*	-0.4358
Middle Aged Security Guards			
Attention ∞ TC	0.0187	*	-0.4338
Attention ∞ LDL	0.0360	*	-0.3909
Executive Function ∞ TC	0.0368	*	-0.5475
Executive Function ∞ LDL	0.0077	**	-0.6709

0.5475, p = 0.0368) and LDL cholesterol (r = -0.6709, p = 0.0077). These findings highlight the potential impact of cholesterol levels on cognitive functions in middle-aged adults.

DISCUSSION

In our cross-sectional study, we examined the correlation between serum lipid parameters and cognitive performance, utilizing qEEG (software Neuroguide) to assess cognitive function in young and middle-aged security guards in Iran. Our findings indicated that TC, LDL, and HDL are significant lipoproteins associated with specific cognitive indices. Notably, executive function and attention were found to have stronger correlations with serum lipoproteins. These results underscore the importance of lipid profiles in relation to cognitive abilities in this population.

In employing security guards as a statistical population, it is crucial to recognize the pivotal role they play in maintaining safety and security within various settings. Security guards serve as the frontline defense against potential threats, ensuring the protection of individuals, property, and sensitive information. By studying security guards as a statistical population, researchers can gain valuable insights into the specific cognitive abilities that are essential for optimal job performance in this demanding role. Understanding the cognitive profiles of security guards can lead to more targeted recruitment strategies, tailored training programs, and enhanced organizational cooperation. Furthermore, by elucidating the relationship between cognitive abilities and job performance in security guards, this research contributes to a broader understanding of how cognitive skills impact performance in complex occupations, ultimately paving the way for improved practices and outcomes in the field of security management (8-10)

High levels of TC and LDL have been identified as established risk factors for cardiovascular disease and have also been linked to cognitive decline (37, 38). These findings suggest that elevated cholesterol levels may have potential negative impacts on cognition, highlighting the importance of managing cholesterol levels to support cognitive health (39). The build-up of cholesterol in blood vessels can lead to atherosclerosis, restricting blood flow to the brain and impairing cognitive function (33). Although peripheral cholesterol cannot enter the central nervous system because of the blood–brain barrier, it reflects the supplement of cholesterol (40). Crucially, cholesterol is an important component of nerve cell membranes and also participates in the metabolic activities of nerve cells. Another factor is that cholesterol stores a large amount of energy, which can be sustainably provided to the brain for a long time, and the brain is the most energy-consuming organ of the body (41). Additionally, the role of cholesterol in brain protection might be different from its role in cardiovascular diseases. Cholesterol is involved in the formation of beta-amyloid plaques associated with Alzheimer's disease, and it may impact the integrity of cell membranes in the brain, affecting neuronal communication (42). Studies have suggested that the accumulation of cholesterol in neurons contributes to amyloid deposition in the brain, potentially accelerating the cleavage of amyloid precursor proteins into amyloidogenic components (43). Furthermore, higher LDL-C has been associated with an increased risk for incident vascular dementia (44). The relationship between serum lipids, brain lipids, and cognition is complex and interconnected, involving cholesterol metabolites, proinflammatory mediators, and antioxidant processes that can impact brain signaling and cognition (45). Interestingly, in our study both TC and LDL levels showed a strong negative correlation with participants' executive functions. Moreover, in the middle age group, these levels were associated with attention. Our findings support the consistent evidence from multiple studies demonstrating the negative impact of elevated TC LDL levels on cognitive function. In a Chinese case–control study involving 227 participants, plasma TC, TG, and HDL levels were found to be associated with the risk of mild cognitive impairment (MCI) (46). Another cross-sectional study in China revealed that individuals with high levels of TC and LDL, but not HDL and TG, were at risk for cognitive impairment (39). Additionally, research in animals and humans has indicated a relationship between cholesterol levels and memory, with disturbances in cholesterol metabolism potentially leading to various cognitive effects (47). Furthermore, a study involving 13,997 participants from the Atherosclerosis Risk in Communities study found that elevated TC and LDL-C levels in midlife were associated with greater 20-year cognitive decline (16). These findings collectively underscore the consistent evidence linking higher TC and LDL-C levels to negative effects on cognition.

Previous research has highlighted the beneficial role of HDL in cognitive function, with higher levels of HDL-C being associated with better cognitive performance. For example, a cross-sectional study in central New York involving 540 elderly individuals demonstrated that those with higher levels of HDL-C scored much better on cognitive tests such as the Mini-Mental State Examination (MMSE) and working memory (48). Similarly, a study in Western Australia found that HDL-C delayed the onset of Alzheimer's disease and dementia, and positively influenced verbal episodic memory, as indicated by performance on the California Verbal Learning Test (CVLT) (15). Another study, revealed a positive association between HDL and cognitive function, particularly in male individuals. This was supported by significant findings from multiple linear regression analysis, demonstrating a link between HDL levels and MMSE scores (49). In contrast, a Chinese longitudinal study involving 2291 participants aged over 60 years found no substantial relationship between HDL and cognitive decline during the follow-up period (50). Our research findings reveal a significant negative association between HDL levels and attention, while no significant correlations were found with other cognitive indices that were measured.

The relationship between triglycerides and cognitive indicators has yielded conflicting results, with some studies showing a positive relationship (19), some showing an inverse relationship (20, 21) , and others finding no relationship at all (22, 23). In our study there was no relation between TG levels and cognitive function such as memory, attention, salience, executive function, language ability and mood.

For further evaluation, we categorized lipoprotein levels as optimal, intermediate, and high, and then conducted a correlation test between each category and cognitive parameters. We hypothesized that high levels of TC and LDL may have been related to executive function and attention, but we found that only the optimal LDL group showed a strong correlation with executive function. Surprisingly, in the other tertiles, intermediate HDL and TGs subsequently had a negative and strong correlation with attention, salience, and mood.

Finally, the study revealed significant negative correlations between executive functions and both total cholesterol (TC) and LDL cholesterol, indicating a potential influence on cognitive performance. Additionally, attention showed significant negative correlations with HDL cholesterol. Furthermore, in the middle-aged adult group, attention demonstrated significant negative correlations with both TC and LDL cholesterol. Similarly, executive function showed significant negative correlations with TC and LDL cholesterol. These findings highlight the potential impact of cholesterol levels on cognitive functions in middle-aged adults.

Differences in findings on the link between lipoproteins and cognitive function may be due to variations in normal ranges of lipoproteins and participant characteristics. Most studies focus on the elderly, suggesting a potential difference in the association across age groups, particularly in younger individuals. Further research is needed to better understand the complex relationship between cholesterol and cognitive function, considering the impact of age and participant characteristics.

The study has several limitations that need to be acknowledged. Firstly, the small sample size may impact the study's robustness, and further larger studies are necessary to provide more conclusive evidence regarding the relationship between plasma Lipoproteins and Cognitive performance. Secondly, the cross-sectional study design prevents the exploration of any causality of plasma lipids with cognitive function. Lastly, the findings should be generalized with caution, as our participants have specific jobs that may affect their cognition and conversely, and it is important to note that all participants in this study were men. Future research should consider including participants from different jobs, and population-based studies are needed to verify the findings.

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DECLARATIONS

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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