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Effects of plasma lipids and smoking on cognitive function

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Aim: To research the relations between plasma lipids and smoking as they affect cognitive functions. Some studies have suggested a relationship between plasma cholesterol concentration, smoking, and the frequency of cognitive disturbances. Our hypothesis was that plasma lipids and smoking are related to cognitive impairment.

Materials and methods: The plasma lipid profiles and cognitive functions of the subjects were measured and the relations among plasma lipid levels, smoking, and cognitive functions were observed. The study was performed on subjects with no history of chronic disease. Mental status was evaluated by the mini-mental state examination (MMSE) in patients over 40 years of age at the Family Medicine Clinic.

In the statistical analyses, Mann-Whitney U, logistic regression, Pearson correlation, and factorial ANOVA tests were used.

Results: Increased total cholesterol (TC), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and low-density to high-density lipid ratios (LDL/HDL) were associated with reduced mental test scores, while high-density lipoprotein (HDL) levels were correlated with improved cognitive function. The negative relation between LDL and cognitive function was more relevant in smokers. Age was negatively related in both genders, whereas educational status was positively related, particularly in women. There was a negative correlation between LDL and language scores on the MMSE and this relation was more relevant in smokers. The mean LDL and LDL/HDL scores of the "24 points and lower" group for total MMSE scores were statistically higher than those of the "over 24" group.

Conclusion: We concluded that for individuals with higher TC, VLDL, LDL, and LDL/HDL ratio levels and/or lower HDL levels, mental functions should be followed carefully, especially in smokers.

Key words: Smoking, cognitive function, low-density lipoprotein, high-density lipoprotein, mental status

Plazma lipidlerinin ve sigara içmenin kognitif fonksiyon üzerine etkileri

Amaç: Bazı çalışmalarda, plazma kolesterol konsantrasyonu ve sigara içmenin, kognitif bozuklukların sıklığı ile olan ilişkisi göstermiştir. Bizim hipotezimiz, "plazma lipidleri ve sigara içmek kognitif bozuklukla ilişkilidir" idi. Çalışmamızda plazma lipidlerinin ve sigara içmenin kognitif fonksiyonlar ile ilişkilerini gözlemeyi hedef edindik.

Yöntem ve gereç: Kişilerin plazma lipid seviyeleri ve kognitif fonksiyonları ölçüldü ve plazma lipid düzeyleri, sigara içme ve kognitif fonksiyonları arasındaki ilişkiler gözlendi. Çalışma, kronik hastalığı olmayan kişilerde uygulandı. Mental durum, Aile Hekimliği kliniğinde 40 yaşın üzerindeki hastalarda mini-mental test (MMSE) ile değerlendirildi. İstatistiksel analizde Mann-Whitney U, logistic regression, Pearson correlation ve factorial ANOVA testleri kullanıldı.

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Bulgular: Total kolesterol, LDL kolesterol, VLDL kolesterol, LDL/HDL oranındaki artma ile mental test skorlarındaki azalma ilişkili iken HDL seviyesi ve kognitif fonksiyondaki iyileşme korele idi. LDL ve kognitif fonksiyon arasındaki negatif ilişki, sigara içenlerde daha belirgin idi. Yaş faktörü, her iki cinste negatif, eğitim durumu ise özellikle kadınlarda mental fonksiyonlar üzerine pozitif ilişkili idi. LDL ile dil puanları arasında negatif bir korelasyon vardı ve bu ilişki özellikle sigara içenlerde daha belirgin idi. Toplam mental skoru 24 ve daha düşük olan grubun LDL ve LDL/HDL oranları, 24 den fazla puan alanlarınkinden daha yüksek idi.

Sonuç: Total kolesterol, VLDL, LDL ve LDL/HDL oranları yüksek olan ve/veya HDL düzeyleri düşük olan kişilerin mental fonksiyonları, özellikle sigara içenlerde daha dikkatli takip edilmelidir.

Anahtar sözcükler: Sigara içme, kognitif fonksiyon, düşük dansiteli lipoprotein, yüksek dansiteli lipoprotein, mental durum

Introduction

Human cognition is among the most important forces in modern life. It enables us to cope with daily complex problems and develop our future plans. Deficits may occur in cognitive abilities such as attention, learning, memory, and planning functions due to both aging and mental disorders. These impairments may destroy our social functions (1).

Areas of cognitive function may be tested. Attention, memory, language, calculations, praxis, judgment, and relations have been studied (2). These areas are classically formulated as orientation, registration, attention and calculation, recall, and language, as well. Orientation is a preferential process in which some signals are selected from others (3). This process continues later with the analysis of the data. Hence, features such as place, subject, and time are recognized by means of their special sites in the brain, and the person realizes what kind of a situation he is in at macro and micro levels. Recall is the ability of protecting and using the acquired knowledge of a living organism (4). This is closely related to learning. Initial acquisition of the knowledge and learning to demonstrate that the knowledge is still retained later is valid in that case. Filtration of the knowledge to lead to behaviors directed to the target is essential for sustaining life. There is an important effectiveness between the attention occurring in such a way and action-based presentations (5). In the language function, even setting out a simple sentence requires a complex mechanism. Initially, the speaker should formulate the composition of his message or his intentions. Consequently, the formulated intention should be realized as a specific language for the communication. This process is a cognitive function, which is performed in a wide area located in both hemispheres (6).

Some basic factors may influence the screening of cognition. These are age, educational level, ethnicity, and primary language (2). Different studies have been conducted related to various situations affecting cognitive functions. For instance, the effects of serum lipid levels, which influence humans of all ages, are very influential. Saturated fat, hydrogenated fat, and cholesterol were reported to impair recall function and morphology of the hippocampus (7). In another study, serum cholesterol levels were shown to lessen the recall function in the elderly (8). The polar metabolite of cholesterol (24-hydroxy cholesterol) was noted to have neurotoxic effects in rats, to cause neuronal damage with abnormal accumulation, and to harm the function of cognition (9). High levels of total cholesterol and oxysterols were accepted as the early markers of cognitive decline in the elderly (10). In a study in which criteria of the national cholesterol education program were utilized as the marker of metabolic syndrome, it was emphasized that metabolic syndrome was associated with global cognitive functions in middle-aged and elderly subjects (11). On the other hand, HDL cholesterol was stated to play a protective role against amnesia (12). Low levels of HDL were stated to be a risk factor for the lessening and deficit of recall in middle-aged adults in another study (13).

In addition to studies on the effects of lipid levels on cognitive functions, other studies related to the effects of smoking, a common habit of people in daily life, on cognitive functions have also been conducted. Smoking was declared to cause a decline in working memory in some studies and has been held responsible for reduced cognitive functions (14). In adolescents, cessation of smoking has improved cognitive functions (15). Furthermore, in university students, mental disorders have been

found more frequent among those who smoke at least 10 cigarettes per day (16).

How do we measure cognitive functions? Cognitive functions are practically tested by Folstein's mini-mental status examination test (MMSE). This device is also useful for the screening of dementia. Dementia is a syndrome that affects the functions of the central nervous system. It is characterized by 3 major symptoms: cognitive disturbance, behavioral disturbance, and disturbance at work or in social activities and relationships. Further evaluations of psychiatric symptoms, personality changes, problematic behaviors, and changes in day-to-day functioning are needed to understand the mechanism of dementia (17). Although these changes have been considered part of normal aging, dementia has been concluded to be an important cause of death in the elderly (18). The most frequent cause of dementia is Alzheimer's disease (AD), in two-thirds of all cases (19). Age seems to be an important risk factor for AD (20). According to a study conducted in Turkey, the prevalence of AD is 11% among those older than 70 years in the Turkish population (21). Serum lipoproteins affect cognitive functions and furthermore may be effective in the pathogenesis of AD (22,23). In some studies, cholesterol and a beta-amyloid protein were found to be related to the pathogenesis of AD (24-27). Serum lipid profiles have also been studied in patients with AD. Elevation of TC, LDL, TG with normal HDL, and the TC/HDL ratio were observed (28).

As we discussed previously, hyperlipidemia is strongly related to cognitive functions. For this reason, we may make the hypothesis that hyperlipidemia, somehow, may lead to cognitive disorders and consequently to dementia. Our primary question is: are serum lipid levels correlated with cognitive functions, and which of them have positive and which have negative effects? The secondary question is: dose smoking affect cognitive functions? The aim of this study was to investigate the relationships among the plasma lipid profile, smoking, and Folstein's MMSE, which is utilized in the screening of cognitive impairment (29-31). We used the modified version of this test by Molloy and Standish, translated into Turkish (32,33). The study was designed to examine whether these variables were related, and, if so, which lipid fractions affect which parts of the MMSE on the basis of smoking status.

Materials and methods

Subjects

This was an observational, case-controlled (normal-high, smoking-nonsmoking) analytical study. Data on subjects of 40 years of age and older were collected. The subjects presented to our hospital for check-up or daily health problems. Upon receiving the institutional ethics consent, the study was conducted at the Family Medicine clinic of the Fatih University School of Medicine in Ankara between 2003 and 2008. The subjects were randomly selected. Randomization was performed by a voluntary acceptance situation for procedures of which preliminary data were suitable for the study. The steps of the study were explained to the selected subjects who accepted the MMSE procedure and were included in the study. Participants were subjected to a detailed history and physical examination, meanwhile giving informed consent for the study.

Blood examination

Lipid profiles were studied by spectrophotometric analysis of the plasma samples obtained after 8 h of fasting. The samples were analyzed in the biochemistry laboratory, which is periodically referenced by international laboratories. The normal levels for both TC and triglyceride were up to 200 mg/dL. The laboratory personnel were blinded to the standardized mental test results. Case and control groups were constituted for each lipid fraction (high = case, normal = control). The ages, educational levels (years of schooling), and MMSE fractions of the case and control groups were compared.

The smoking status (smoking and nonsmoking) of the subjects was also recorded. All of the subjects were administered the MMSE. The person applying the test was blinded to the lipid profile results.

Inclusion/exclusion criteria

Individuals of 40 years of age or older who had no conditions that might affect cognitive functions were included. All lipid-lowering therapies and any history of a disease or condition that might affect cognitive function (known vascular, neurologic,

endocrine, or psychiatric diseases; drug usage; etc.) were considered as exclusion criteria. Age, gender, educational status, lipid profiles, and MMSE scores of all subjects were recorded. The MMSE scores were evaluated for the following categories: orientation (10 points), registration (3 points), attention and calculation (5 points), recall (3 points), language (9 points), and total (30 points).

Statistical analysis

Statistical analyses were performed to determine the effects of age, educational status, smoking status, and lipid profiles on the MMSE results. The Mann-Whitney-U test and Student's t-test were used for comparison of categorical data; the means of continuous measurements were compared to determine differences. The independent samples test was used to compare each of the parameters of the MMSE in 2 groups for all lipid fractions for cut-off values. Furthermore, categorical comparisons of multiple lipid fractions and the above ratios for meaningful total MMSE points (24) were performed. Multivariate analyses (correlation, factorial ANOVA, and logistic regression) for age, educational status, lipid profile parameters, and MMSE were also performed. Factorial ANOVA was used to determine possible combined effects of age, educational level, smoking, and lipid fractions on the cognitive functions. Any P value of <0.05 was considered to indicate statistical significance; all tests were 2-tailed and in the 95% confidence interval. All statistical analyses were performed on a personal computer with the statistical package SPSS 13.0 for Windows.

Results

General features of the cases

A total of 117 subjects were evaluated in this study. For various reasons, 29 were excluded (6 for hypertension, 3 for diabetes mellitus, 5 for vitamin B12 deficiency, 8 for depression, 3 for neurologic disease, and 4 for use of medications that affect the central nervous system). Thus, 88 subjects were finally included in the study, 38 males and 50 females. The mean age of the subjects was 54.8 ± 9.8 years, and the mean length of education was 6.6 ± 4.2 years. The total MMSE scores for each gender group were determined. In the males, the mean score was 27.47 ± 2.1, and in the females, 25.74 ± 3.6. Other features are outlined in Table 1.

Total cholesterol levels and mental status

TC levels higher than 200 mg/dL were considered "high." The language scores of the "normal" cholesterol group were generally statistically significantly higher than those of the "high" group (means: 8.41 ± 0.89 versus 7.84 ± 1.5, P = 0.037). In the gender groups, the language scores of the "normal" group were statistically significantly higher than those of the "high" group for males (Table 1). In the same group, a negative correlation was found between the total cholesterol and language scores (R = -0.334, N = 38, P = 0.041).

As pointed out in the previous paragraphs, educational level and age may also affect cognitive functions. The relationships between total cholesterol levels and other variables of the MMSE were also evaluated. Thus, pure effects of lipid fractions on cognitive function were investigated and factorial ANOVA analysis was performed to estimate possible effects of age, educational level, and smoking. A significant relationship was generally found among TC and language scores (Table 2).

Lipid fractions and mental status

For each lipid fraction, a cut-off level for a more significant relation was determined. We analyzed each group's scores by independent samples tests. We observed further combined relations among lipid fraction categories (LDL, VLDL, and HDL), age, years of education, smoking status, and MMSE test results by factorial ANOVA.

Low-density lipoprotein levels and mental status

The mean language scores of the "130 and lower" LDL group were statistically higher than those of the "higher than 130" LDL group for the entire study population (Table 3). Pure effects of lipid fractions on cognitive function were investigated and factorial ANOVA analysis was performed to estimate the possible effects of age, educational level, and smoking status. Further evaluation was conducted to determine any relationship between LDL category and cognitive function. LDL category and language scores were generally significantly related, according to factorial ANOVA results (Table 4). This significant

Table 1. Descriptive comparisons of parameters of total cholesterol groups.

Parameter	Group 1		Group 2		P
	N	Mean	N	Mean	
Age					
Men	21	58.2 ± 7.9	17	57.8 ± 7.8	NS
Women	23	51.4 ± 10.6	27	53 ± 10.8	NS
Educational years					
Men	21	8.6 ± 3.7	17	7.8 ± 3.9	NS
Women	23	4.4 ± 3.8	27	6 ± 4.3	NS
Orientation					
Men	21	9.8 ± 0.36	17	9.8 ± 0.3	NS
Women	23	9 ± 1	27	9.3 ± 1.2	NS
Registration					
Men	21	3 ± 0	17	3 ± 0	NS
Women	23	2.9 ± 0.2	27	2.9 ± 0.2	NS
Attention and calculation					
Men	21	4.3 ± 1.2	17	4.3 ± 1.2	NS
Women	23	3.6 ± 1.8	27	3.4 ± 2	NS
Recall					
Men	21	1.8 ± 0.9	17	2 ± 0.86	NS
Women	23	1.9 ± 0.8	27	2.2 ± 0.8	NS
Language					
Men	21	8.7 ± 0.5	17	7.8 ± 1.6	0.037*
Women	23	8.1 ± 1	27	7.8 ± 1.4	NS
Total					
Men	21	27.8 ± 1.6	17	27 ± 2.5	NS
Women	23	25.7 ± 3.2	27	25.8 ± 3.9	NS

Group 1: 200 and below, Group 2: above 200

relationship between LDL category and language scores was more relevant among males (P = 0.023).

Generally, there was a negative correlation between LDL levels and language (Pearson correlation = -0.210, N=88, P = 0.049) (Figure). However, separate evaluation of these values for each smoking status category showed that there was a negative correlation between LDL levels and language in the smoking group (Pearson correlation = -0.564, N = 14, P = 0.035).

Very low-density lipoprotein levels and mental status

The mean registration scores of the "40 and below" VLDL group were generally statistically higher than those of the "higher than 40" VLDL group (Table 3). There was also generally a significant relation

Table 2. Relations between total cholesterol, age, education, smoking, and MMSE scores. Dependent Variable: Orientation

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	11.641(a)	4	2.910	3.435	0.012
Intercept	120.861	1	120.861	142.668	<0.001
Smoking	2.191	1	2.191	2.586	0.112
Age	0.002	1	0.002	0.002	0.963
Years of Ed.	9.110	1	9.110	10.753	0.002
Tot. Cholest.	0.019	1	0.019	0.023	0.880
Error	70.313	83	0.847		
Total	7986.000	88			
Corrected Total	81.955	87			

a: $R^2 = 0.142$ (Adjusted $R^2 = 0.101$)

Dependent Variable: Recall

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	17.713(a)	4	4.428	7.619	<0.001
Intercept	25.399	1	25.399	43.699	<0.001
Smoking	1.715	1	1.715	2.951	0.090
Age	14.352	1	14.352	24.693	<0.001
Years of Ed.	0.004	1	0.004	0.008	0.930
Tot. Cholest.	0.323	1	0.323	0.556	0.458
Error	48.241	83	0.581		
Total	426.000	88			
Corrected Total	65.955	87			

a: $R^2 = 0.269$ (Adjusted $R^2 = 0.233$)

Dependent Variable: Language

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	17.464(a)	4	4.366	2.872	0.028
Intercept	159.054	1	159.054	104.640	<0.001
Smoking	0.031	1	0.031	0.020	0.887
Age	5.346	1	5.346	3.517	0.064
Years of Ed.	7.071	1	7.071	4.652	0.034
Tot. Cholest.	6.103	1	6.103	4.015	0.048
Error	126.161	83	1.520		
Total	5953.000	88			
Corrected Total	143.625	87			

a: $R^2 = 0.122$ (Adjusted $R^2 = 0.079$)

Table 3. Comparisons of the MMSE scores to lipid groups within cases.

Parameter	Group 1		Group 2		P
	N	Mean	N	Mean	
Orientation					
VLDL	63	9.59 ± 0.73	25	9.2 ± 1.38	NS
HDL	53	9.3 ± 1	35	9.6 ± 0.6	NS
LDL	59	9.3 ± 1	29	9.7 ± 0.7	NS
Registration					
VLDL	63	3 ± 0	25	2.9 ± 0.27	0.024 (0.009*)
HDL	53	2.9 ± 0.13	35	2.9 ± 0.16	NS
LDL	59	2.9 ± 0.2	29	2.5 ± 0.9	NS
Attention and calculation					
VLDL	63	3.9 ± 1.6	25	3.7 ± 1.8	NS
HDL	53	3.5 ± 1.8	35	4.4 ± 1.3	NS (0.020*)
LDL	59	3.8 ± 1.7	29	3.9 ± 1.7	NS
Recall					
VLDL	63	2 ± 0.9	25	2 ± 0.79	NS
HDL	53	2 ± 0.8	35	1.9 ± 0.9	NS
LDL	59	2 ± 0.8	29	2 ± 0.9	NS
Language					
VLDL	63	8.1 ± 1.3	25	8.1 ± 1.2	NS
HDL	53	8 ± 1.3	35	8.2 ± 1	NS
LDL	59	8.3 ± 1	29	7.7 ± 1.4	0.034 (0.036*)
Total					
VLDL	63	26.6 ± 2.9	25	26 ± 3.5	NS
HDL	53	26 ± 3.5	35	27 ± 2.3	NS (0.014*)
LDL	46	26.5 ± 3.2	12	26.4 ± 3	NS

VLDL: Group 1, 40 and below; Group 2, higher than 40
LDL: Group 1, 130 and below; Group 2, higher than 130
HDL: Group 1: 50 and below; Group 2, higher than 50
*P-values of multiple comparisons in the corrected model

between VLDL category and registration scores by factorial ANOVA (Table 4).

High-density lipoprotein levels and mental status

The mean attention and calculation scores of the "higher than 50" HDL group were generally higher than those of the "50 and below" group (Table 3). This relation was never significant statistically by direct comparison; however, we observed a significant relation between HDL category and attention and calculation scores by the corrected model (factorial ANOVA) (Table 4).

Based on the results of factorial ANOVA, relations between lipid fraction categories (LDL, VLDL, and

Table 4. Relations between lipid fraction categories, age, education, smoking, and MMSE scores.

Dependent Variable: Registration

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	0.188(a)	6	0.031	1.439	0.210
Intercept	13.595	1	13.595	623.440	<0.001
Smoking	0.026	1	0.026	1.213	NS
Years of ed.	0.001	1	0.001	0.047	NS
Age	0.012	1	0.012	0.549	NS
HDL Category	0.025	1	0.025	1.152	0.286
LDL Category	0.003	1	0.003	0.133	0.716
VLDL Category	0.158	1	0.158	7.229	0.009
Error	1.766	81	0.022		
Total	782.000	88			
Corrected Total	1.955	87			

a: $R^2 = 0.096$ (Adjusted $R^2 = 0.029$)

Dependent Variable: Attention and Calculation

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	24.347(a)	6	4.058	1.383	0.232
Intercept	6.221	1	6.221	2.120	0.149
Smoking	1.935	1	1.935	0.659	0.419
Years of Ed.	6.879	1	6.879	2.344	0.130
Age	0.104	1	0.104	0.035	0.851
HDL Category	16.646	1	16.646	5.672	0.020
LDL Category	0.075	1	0.075	0.026	0.873
VLDL Category	0.341	1	0.341	0.116	0.734
Error	237.732	81	2.935		
Total	1599.000	88			
Corrected Total	262.080	87			

a: $R^2 = 0.093$ (Adjusted $R^2 = 0.026$)

Dependent Variable: Language

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	21.372(a)	6	3.562	2.360	0.038
Intercept	122.826	1	122.826	81.380	<0.001
Smoking	0.615	1	0.615	0.408	0.525
Years of Ed.	6.543	1	6.543	4.335	0.040
Age	7.356	1	7.356	4.874	0.030
HDL Category	3.696	1	3.696	2.449	0.122
LDL Category	6.860	1	6.860	4.545	0.036
VLDL Category	0.344	1	0.344	0.228	0.634
Error	122.253	81	1.509		
Total	5953.000	88			
Corrected Total	143.625	87			

a: $R^2 = 0.149$ (Adjusted $R^2 = 0.086$)

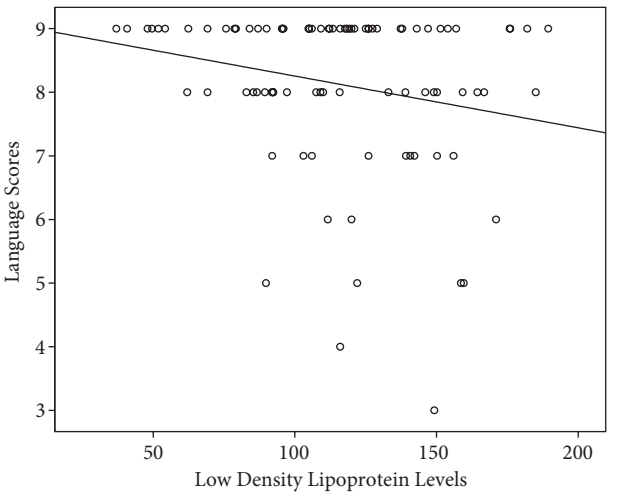

Figure. Negative correlation between LDL levels and language scores.

HDL), age, educational years, smoking status, and total MMSE scores were determined. We observed a significant relation between HDL category and total scores with the corrected model (Table 5). The cut-off point of MMSE (24) results for suspected levels of dementia and relations between the above factors were also investigated by logistic regression analysis. With that method, we observed a significant relation between total MMSE score for suspected dementia and HDL category (P = 0.013).

Age and mental status

The effects of various factors on cognitive functions were evaluated. Generally, significant relations between age and recall scores, between age and language scores, and between age and total scores were determined by factorial ANOVA (Tables 2, 4, and 5). Furthermore, there was a negative correlation between age and recall scores (R = -0.367, N = 88, P < 0.001). In the gender groups, there were negative correlations between age and total MMSE scores and between age and recall scores for the males (R = -0.399, -0.430; N = 38; P = 0.013, 0.007), and there was a negative correlation between age and recall scores for the females (R= -0.294, N = 50, P = 0.038).

Education level and mental status

Some studies have shown that low educational status constitutes a risk factor for cognitive

Table 5. Relations between lipid fraction categories, age, education, smoking, and total MMSE scores.

Dependent Variable: Total

Source	Type-III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	176.580(a)	6	29.430	3.458	0.004
Intercept	1111.528	1	1111.528	130.593	<0.001
Smoking	34.259	1	34.259	4.025	NS
Years of Ed.	64.612	1	64.612	7.591	0.007
Age	49.348	1	49.348	5.798	0.018
HDL Category	53.738	1	53.738	6.314	0.014
LDL Category	.886	1	0.886	0.104	NS
VLDL Category	1.288	1	1.288	0.151	NS
Error	689.420	81	8.511		
Total	62664.000	88			
Corrected Total	866.000	87			

a: $R^2 = 0.204$ (Adjusted $R^2 = 0.145$)

impairment and AD (34). Generally, significant relations were observed between years of education and orientation scores, between years of education and language, and between years of education and total scores (Tables 2, 4, and 5). Furthermore, positive correlations were generally found between years of education and orientation (R = 0.304, N = 88, P = 0.004), years of education and language (R = 0.251, N = 88, P = 0.018), and years of education and total scores (R = 0.293, N = 88, P = 0.006). These positive correlations were more relevant among females for years of education and orientation (R = 0.344, N = 50, P = 0.015) and for years of education and total scores (R = 0.299, N = 50, P = 0.035).

Discussion

Comparison with previous findings

Negative relations between cognitive functions (especially recall function) and cholesterol levels were noted in previous studies (7-9). The separate relations between TC as well as lipoprotein fractions and cognitive functions were evaluated in our study, finding negative relations between some lipid fractions and some cognitive functions. However, TC was negatively related with language scores. The negative relationship of TC with language was observed particularly in males. LDL also had a negative relationship with language, and VLDL and registration scores were likewise negatively related. Smoking was found to be associated with a decrease in working memory in previous studies (14). In our study, results on LDL and language scores were most markedly correlated in the smoking group.

Positive effects of HDL cholesterol on cognitive functions were emphasized in some earlier studies, and low levels of HDL were noted to be a risk factor for cognitive impairment (12,13). In our study, positive correlations of mental test scores with lipid fractions were observed only for HDL. Generally, HDL levels were positively correlated with attention and calculation scores and total scores in the corrected model. The cut-off point was 50 for HDL. Thus, some mechanisms of plasma lipid elevation and reflections of this elevation into the brain may initially affect cognitive function to some extent (neuronal conduction changes, brain metabolism changes, etc.), or metabolic disturbances may affect both lipid metabolism and brain functions. These effects seem more pronounced in the aging process. However, positive effects of HDL may be due to influences of an active lifestyle or healthy lipid metabolism.

Sparks et al. have observed lipid profiles in AD as showing elevations in the TC, TG, and LDL levels and normal HDL and TC/HDL levels (28). In our study, among groups with lower and normal scores of total MMSE, respectively, mean TC levels were 215.6 ± 36.6 and 197.4 ± 42.8, mean VLDL levels were 35.8 ± 15.8 and 35.6 ± 23.8, mean LDL levels were 130.5 ± 29.6 and 112.3 ± 35.6, mean TC/HDL levels were 4.5 ± 0.8 and 4.2 ± 1.5, and mean LDL/HDL levels were 2.7 ± 0.6 and 2.4 ± 1.

Ratios of subjects with lower total MMSE scores were higher than those of subjects with higher total MMSE scores. Meanwhile, HDL was slightly lower in subjects with lower scores (49.17 ± 14.7 versus 49.28 ± 12.8). However, we observed statistical significance for only LDL (at P = 0.038) and the LDL/HDL ratio (P = 0.05). Strikingly, negative correlations were found between various MMSE fractions and the above mentioned lipid fractions. In the corrected model and the logistic regression analysis, HDL was the most influential lipid fraction on total cognitive function. The combination of negative effects of LDL, especially in smokers, and the positive effects of HDL together were the most striking by calculation of ratios. Initially, negative effects of LDL on MMSE fractions were enforced by increasing LDL/HDL ratios and ultimately were effective on the total MMSE scores, meaningful for the dementia threshold.

Advanced age affected total MMSE results negatively for both genders, and higher educational status affected total MMSE results positively, especially for women. These results were parallel to the literature reporting psychosocial risks of AD (34). No correlations were found between age and lipid fractions or between educational status and lipid fractions.

In some studies, smoking was pointed out as a risk factor for cognitive decline (15,16). In our study, smoking alone did not have any effect on cognitive function. However, the negative effects of LDL on

the language scores were enforced by smoking. Thus, it can be said that high lipid levels may constitute a higher risk for cognitive decline among smokers.

Clinical implications

The effects of lipids on cognitive function should be evaluated by observational and experimental studies. Neuronal conduction speeds, lipid fractions of neuronal structures, relationships between changes of these fractions and neuronal functions, and effects of these changes in different parts of the brain may be observed, especially in smokers. In addition, the effects of lipid-lowering therapies and differences of these effects among various drugs, and the effects of cessation of smoking, should be explored for positive effects on cognitive function in detailed studies. The LDL/HDL ratio should be calculated and total MMSE scores for subjects with increased values should be followed carefully. Some lifestyle changes may be useful for increasing HDL.

Study limitations

The study involved a limited number of subjects. Nevertheless, some striking relationships were found between various lipid fractions and cognitive function, and some of them were correlated with the results of previous reports. Future multicenter studies with larger series are needed before generalizing these results for routine medical practice.

Conclusions

Increased TC, LDL, VLDL, and LDL/HDL ratios were associated with reduced mental test scores, but HDL levels were positively correlated with cognitive function. LDL was an especially strong risk factor in smokers; age was effective in both genders, whereas educational status was especially effective in women. We conclude that in the subjects with higher LDL (particularly smokers), higher LDL/HDL levels and lower HDL levels should be followed carefully for the risk of declining cognitive function.

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