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Cognitive functions, lipid profile, and Apolipoprotein E gene polymorphism in postmenopausal women

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Abstract

The objective of the study was investigation of the relationship between cognitive functions and lipid profile, BMI and change of body weight in postmenopausal women carriers of Apolipoprotein E gene polymorphisms (APOE). A group of 170 women was recruited to the study. The inclusion criteria were: minimum of two years after the last menstruation, FSH concentration 30 U/ml and no signs of dementia on the Montreal Cognitive Assessment (MoCA). A computerized battery of Central Nervous System Vital Signs (CNS VS) was used for diagnostic cognitive functions. APOE genotype was performed by multiplex PCR. In blood plasma were determined: triglycerides, total cholesterol and its fractions: HDL cholesterol and LDL cholesterol. Statistical analysis was performed using two-way analysis of variance in STATISTICA software. In the postmenopausal women examined, the carrier state of APOE gene polymorphism was associated with the level of triglycerides, and results concerning three cognitive functions: executive functions, psychomotor speed, and cognitive flexibility. Loss of body weight in postmenopausal women was related with lower results in neurocognitive index and the majority of cognitive functions. The results concerning cognitive functions in postmenopausal women in the study were not significantly related with lipid profile. Significant differences were observed according to APOE gene polymorphism in correlations between LDL/HDL and CHOL/HDL ratios, and results in the processing speed and reaction time, as well as between the BMI and results in processing speed in the postmenopausal women examined.

Key words

menopause, cognitive functions, lipids, apolipoprotein E gene

INTRODUCTION

Many reports dealing with the problems of neuropsychology have confirmed that cognitive functions deteriorate with age. It is commonly known that going through menopause exerts a strong effect on the health and life of women, because there occur rapid changes of their hormonal profile, psycho-social and physical functioning [1].

The results of research show that the same factors as in the case of atherosclerotic changes may be responsible for the development of changes of the dementia type. Individuals with a high level of total cholesterol and low-density lipoproteins are at a higher risk of cognitive disorders and dementia at the end of their lives [2]. Metabolic syndrome, which covers abdominal obesity, hypertriglyceridaemia, low HDL cholesterol values, arterial hypertension and/or hyperglycemia, is also associated with an increased risk of cognitive disorders and a decrease in cognitive functions [3]. Several epidemiological clinical studies have been published, supported by histopathologic tests [4], which confirm the vascular hypothesis of the development of dementia. Vascular changes leading to damage of the cerebral white matter are related with a lower efficacy of the frontal lobe of the brain, including the functions of attention, memory and executive functions, cognitive flexibility, emotional processes and processing speed [5, 6]. This is confirmed by a systematic review in which it was found that type 2 diabetes, arterial hypertension, dyslipidaemia, and obesity are associated with a decrease in the cognitive functions, such as: processing speed, cognitive flexibility and memory in individuals who have no symptoms of dementia [7].

Cerebral lipids, such as cholesterol, play an important role in homeostasis of the neuronal membrane and synaptic function. Apolipoprotein E (apoE) is the main protein transporting lipids in the brain. In addition, it is presumed that the apolipoprotein E (APOE) gene located on chromosome 19 is the gene affecting the risk of the development of neurodegenerative changes in the brain [8, 9]. Apolipoprotein E is a polymorphic protein which occurs in humans in three forms of isomorphism: apoE2, apoE3, and apoE4, coded by the *three alleles* for the *APOE gene,* three allelic systems of the APOE gene: ε2, ε3 and ε4. [10, 11]. Individual isoforms of apoE protein differ with respect to their functions. The differences concern lipid and non-lipid apoE effects. It was confirmed that lipid particles containing apoE4 isoform effectively bind LDL receptors,

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which results in a decreased expression of receptors and an increase in the level of lipoprotein in blood plasma. In the situation when apoE2 isoform enters into the composition of lipid particles, they poorly bind LDL receptors, the activity of receptors increases, while the LDL level in blood plasma decreases. Among other effects which may be associated with the development of cognitive function disorders and, consequently, in Alzheimer disease, apoE is engaged in the processes of oxidative damage, activation of microglia and astrocytes, as well as an inflammatory reaction. [12]. The presence of apoE4 also favours the deposition of β-amyloid in the brain which, in combination with the above-described neurodegenerative changes, is a risk factor for the development of cognitive disorders and dementia [13]. Some studies show that the relationship between the BMI and cognitive functions is more complicated, and there is no unequivocal evidence that overweight and obesity are conducive to the development of dementia [14].

Objective. The objective of the study was investigation of the relationship between cognitive functions and lipid profile, BMI and change of body weight in postmenopausal women carriers of Apolipoprotein E gene polymorphisms. The following research problems were posed:

1) Do lipid profile, BMI and change of body weight in postmenopausal women depend on Apolipoprotein E (APOE) gene polymorphism?
2) Do cognitive functions in postmenopausal women depend on APOE gene polymorphism?
3) Do cognitive functions in postmenopausal women depend on lipid profile, BMI, and change in body weight?
4) Do the correlations between cognitive functions and lipid level in postmenopausal women depend on APOE gene polymorphism?

MATERIALS AND METHOD

The study was conducted in 2011 at the Institute of Rural Health in Lublin, Poland, and the study group were women from the south-eastern part of the country. The criteria for inclusion in the study were: age 50–65, good general health, education level – at least completed elementary. The women were qualified into the study group also based on clinical symptoms (minimum 2 years from the last menstrual period) and based on the criterion of FSH level (FSH>30 mlU/ml). The criteria for exclusion from the study were: active cancerous disease within the period of five years after recruitment; mental diseases in medical history, including depressions before menopause, addiction to drugs and alcohol, diagnosed nosologic unit with the symptoms of dementia. At the stage of qualification for the study, a brief MoCA test was conducted in order to include in the study the patients who did not show the features of dementia [15]. 170 postmenopausal women were examined.

Cognitive functions were evaluated using the diagnostic instrument CNS –Vital Signs (Polish version) [16] with software by CNS Vital Signs (Chapel Hill, NC, USA). CNS-VS covers the following tests: Verbal Memory Test (VBM), for examining motor functioning, Finger Tapping Test(FTT), Symbol Digit Modalities Test (SDMT), Stroop Test (ST), Shifting Attention Test (SAT), and Continuous Performance. CNS-VS assesses nine cognitive functions: memory, verbal memory, visual memory, processing speed, executive functioning, psychomotor speed, reaction time, complex attention, and cognitive flexibility. Based on five of these functions – memory, psychomotor speed, reaction time, complex attention, and cognitive flexibility – the Neurocognition Index (NCI) is calculated. The computer data from the CNS-VS test provides raw results, standardized results, percentiles, and evaluations according to the 5-point scale for each of nine cognitive functions examined and the neurocognitive index. These evaluations are as follows: above average (more than 109 standardized scores), average (90–109), low average (80–89), low (70–79), very low (less than 70).

Lipid profile was determined using an automatic biochemistry analyser Express Plus (Chiron Diagnostics, USA), with reagents by Siemens (Siemens Healthcare Diagnostics, Tarrytown, NY, USA), according to the procedure provided by the manufacturer. The following were determined in blood plasma: triglycerides, total cholesterol and its fractions: HDL cholesterol and LDL cholesterol.

Genomic DNA was isolated from whole blood of patients, using commercial kits for isolation of DNA from blood (Qiagen), and the amount and purity of the genetic material isolated was measured using a NanoDrop spectrophotometer. In the study, genotyping methods were applied based on the detection of variations in the nucleotide sequences of alleles of APOE genes (single nucleotide polymorphism, SNP) [17]. For PCR reaction (T-ARMS PCR) and multiplex PCR (T-ARMS PCR) proper polymers for allelic locations were used. Amplification products were detected in agar gels after performing electrophoresis. In order to confirm the results, PCR-RFLP reaction was performed, where the amplification product was subjected to the effect of restriction enzyme *Hha*I, and the products of digestion were visualized on polyacrylamide gels after electrophoresis, which allowed identification of the restriction pattern characteristic for each genotype. In addition, ASPC reaction (Allele Specific PCR) was performed using specific polymers, where amplification products were subjected to electrophoresis, and the results of genotyping compared with the results obtained using all the methods applied. The amplification products obtained were subject to sequencing, and the sequences obtained were compared with the data from the Gene Bank.

Statistical analysis was performed using the software package STATISTICA. In the characteristics of the study sample, lipid levels and cognitive functions (standardized results) (Tab. 1, 2 and 3) arithmetic means were calculated (M) ± standard deviation (SD), and for quantitative characteristics and/or absolute (n) and relative numbers (%) for qualitative characteristics. The significance of the differences in quantitative characteristics between three groups of APOE polymorphism was investigated using analysis of variance F test, whereas the significance of the qualitative characteristics – by means of stochastic independence test χ^2. Analysis of cognitive functions according to body weight after menopause (Tab. 4) covered median (Me) ± quarter deviations (Q), and the significance of the differences in cognitive functions between three groups of APOE polymorphism was examined using H Kruskal-Wallis test, due to the small numbers counts of women with body weight loss after menopause. To investigate correlations between cognitive functions (standardized results) and lipid level (Tab. 5), Pearson correlation coefficient (r) was used. The effect of APOE

Table 1. Characteristics of postmenopausal women in the study in general, and according to APOE gene polymorphism

Characteristics	Parameters	Total (n=170)	APOE 2/3 (n=31)	APOE 3/3 (n=104)	APOE 3/4 or4/4 (n=35)	F or χ^2	p
Age (years)	M±SD	56.4±3.5	56.6±3.5	56.6±3.6	55.9±3.4	F= 0.461	0.633
BMI (kg/m2)	M±SD	26.5±4.1	26.4±4.0	26.8±4.1	25.8±4.3	F= 0.626	0.538
BMI (groups)							
underweight	n (%)	3 (1.76)	0 (0.00)	3 (2.88)	0 (0.00)	χ^2= 4.053	0.669
normal weight	n (%)	62 (36.47)	12 (38.71)	34 (32.69)	16 (45.71)		
overweight	n (%)	71 (41.76)	14 (45.16)	44 (42.31)	13 (37.14)		
obesity	n (%)	34 (20.00)	5 (16.13)	23 (22.12)	6 (17.14)		
Change of body weight after menopause							
no changes	n (%)	56 (32.94)	6 (19.35)	37 (35.58)	13 (37.14)	χ^2= 4.721	0.317
loss	n (%)	11 (6.47)	1 (3.23)	7 (6.73)	3 (8.57)		
increase	n (%)	103 (60.59)	24 (77.42)	60 (57.69)	19 (54.29)		

Table 2. Lipid profile of postmenopausal women examined in general, and according to APOE gene polymorphism

Lipids	Parameters	Total (n=170)	APOE 2/3 (n=31)	APOE 3/3 (n=104)	APOE 3/4 or 4/4 (n=35)	F or χ^2	p
CHOL (mg/dl)	M±SD	228.3±44.0	233.7±44.2	224.8±41.1	234.1±51.8	F= 0.876	0.418
CHOL (normal)	n (%)	27 (15.88)	3 (9.68)	18 (17.31)	6 (17.14)	χ^2= 1.093	0.579
CHOL (above normal)	n (%)	143 (84.12)	28 (90.32)	86 (82.69)	29 (82.86)		
HDL (mg/dl)	M±SD	54.4±12.5	55.1±10.2	53.4±12.3	56.6±14.8	F= 0.875	0.419
HDL (normal)	n (%)	34 (20.00)	6 (19.35)	19 (18.27)	9 (25.71)	χ^2= 0.917	0.632
HDL (below normal)	n (%)	136 (80.00)	25 (80.65)	85 (81.73)	26 (74.29)		
TG (mg/dl)	M±SD	147.6±63.6	149.1±63.3	154.9±65.3	124.5±54.3	F= 3.074	0.049
TG (normal)	n (%)	100 (58.82)	17 (54.84)	57 (54.81)	26 (74.29)	χ^2= 4.350	0.114
TG (above normal)	n (%)	70 (41.18)	14 (45.16)	47 (45.19)	9 (25.71)		
LDL (mg/dl)	M±SD	144.4±45.5	148.8±43.7	140.3±42.9	152.7±53.8	F= 1.140	0.322
LDL (normal)	n (%)	40 (23.53)	4 (12.90)	27 (25.96)	9 (25.71)	χ^2= 0.280	0.304
LDL (above normal)	n (%)	130 (76.47)	27 (87.10)	77 (74.04)	26 (74.29)		
LDL/HDL	M±SD	2.84±1.17	2.79±0.94	2.82±1.18	2.93±1.36	F= 0.150	0.869
LDL/HDL (normal)	n (%)	99 (58.24)	19 (61.29)	58 (55.77)	22 (62.86)	χ^2= 3.861	0.451
LDL/HDL (borderline level)	n (%)	46 (27.06)	7 (22.58)	33 (31.73)	6 (17.14)		
LDL/HDL (high risk)	n (%)	25 (14.70)	5 (16.13)	13 (12.50)	7 (20.00)		
CHOL/HDL	M±SD	4.42±1.34	4.37±1.06	4.44±1.35	4.42±1.53	F= 0.038	0.963
CHOL/HDL (normal)	n (%)	75 (44.12)	13 (41.94)	44 (42.31)	18 (51.43)	χ^2= 2.428	0.657
CHOL/HDL (borderline level)	n (%)	42 (24.71)	10 (32.26)	26 (25.00)	6 (17.14)		
CHOL/HDL (high risk)	n (%)	53 (31.17)	8 (25.80)	34 (32.69)	11 (31.43)		

Table 3. Cognitive functions among postmenopausal women in the study in general, and according to APOE gene polymorphism (mean ± standard deviations in standardized results)

Cognitive functions	Total (n=170)	APOE 2/3 (n=31)	APOE 3/3 (n=104)	APOE 3/4 or 4/4 (n=35)	F	p
NCI	83.8±16.5	89.6±16.6	83.6±14.1	79.4±21.4	2.606	0.083
Memory	89.0±16.2	89.4±17.1	88.9±15.4	89.1±18.2	0.011	0.989
Verbal memory	90.1±18.4	90.5±20.5	89.8±18.0	90.4±18.1	0.026	0.974
Visual memory	92.8±15.4	93.3±12.0	92.8±15.8	92.5±17.0	0.030	0.971
Processing speed	78.7±14.8	79.7±15.9	78.2±15.0	79.4±13.4	0.174	0.840
Cognitive functioning	79.1±25.7	90.0±20.2	79.0±24.0	69.8±31.5	5.579	0.006
Psychomotor speed	83.4±17.6	90.9±14.4	82.0±15.9	81.0±22.9	4.613	0.014
Reaction time	86.6±16.3	90.6±19.4	84.8±15.0	88.4±16.6	1.561	0.219
Complex attention	80.9±31.3	88.9±36.0	82.7±25.9	68.8±38.4	2.627	0.082
Cognitive flexibility	78.0±26.8	88.9±22.5	78.1±24.7	68.1±32.6	4.929	0.010

Table 4. Cognitive functions in postmenopausal women examined in general, and according to change in body mass after menopause (median ± quartile deviations of standardized results)

Cognitive functions	Total (n=170)	Change in body weight after menopause			H	p
		No changes (n=56)	Loss (n=11)	Increase (n=103)		
NCI	86.5±11.5	87.5±10.0	67.0±6.0	89.0±10.0	10.741	0.005
Memory	88.5±11. 0	87.0±12.0	81.0±11.5	91.0±12.5	6.030	0.049
Verbal memory	91.5±15.5	91.5±13.5	80.0±12.5	94.0±14.5	3.579	0.167
Visual memory	94.0±9.5	93.0±9.5	87.0±19.0	96.0±11.5	1.888	0.389
Processing speed	79.5±10.0	80.0±8.5	62.0±6.5	81.0±10.5	13.871	0.001
Cognitive functioning	85.0±19.0	86.0±14.0	62.0±10.0	87.0±19.0	6.377	0.041
Psychomotor speed	86.5±12.0	87.0±8.5	71.0±4.5	88.0±12.5	9.280	0.010
Reaction time	88.0±10.5	89.5±9.3	76.0±13.5	88.0±11.0	4.621	0.099
Complex attention	89.0±17.5	89.5±16.8	60.0±13.0	92.0±17.5	8.849	0.012
Cognitive flexibility	86.0±19.0	86.0±13.0	60.0±14.5	87.0±18.5	7.090	0.029

Table 5. Correlation coefficients between cognitive functions (standardized results), and BMI and lipid levels in postmenopausal women in general

Cognitive functions	Parameters	BMI (kg/m²)	CHOL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	LDL (mg/dl)	LDL/HDL	CHOL/HDL
NCI	R	0.113	0.111	0.057	0.082	0.069	0.014	0.004
	P	0.144	0.151	0.463	0.289	0.375	0.858	0.959
Memory	R	0.125	0.041	0.039	0.015	0.025	-0.004	-0.011
	P	0.105	0.592	0.618	0.849	0.743	0.963	0.887
Verbal memory	R	0.030	0.092	-0.037	0.040	0.089	0.064	0.060
	P	0.694	0.231	0.628	0.606	0.251	0.406	0.435
Visual memory	R	0.192	-0.026	0.090	-0.020	-0.044	-0.058	-0.065
	P	0.012	0.741	0.242	0.794	0.571	0.453	0.401
Processing speed	R	0.065	-0.001	-0.086	0.049	0.009	0.054	0.039
	P	0.399	0.992	0.263	0.529	0.903	0.483	0.611
Executive functioning	R	0.093	0.119	0.033	0.085	0.083	0.030	0.019
	P	0.229	0.121	0.674	0.269	0.284	0.699	0.803
Psychomotor speed	R	0.045	0.038	0.025	0.032	0.021	-0.004	-0.008
	P	0.561	0.621	0.745	0.682	0.784	0.955	0.919
Reaction time	R	-0.005	0.034	0.108	0.050	-0.011	-0.062	-0.068
	P	0.950	0.661	0.160	0.522	0.889	0.426	0.380
Complex attention	R	0.107	0.120	0.076	0.122	0.062	0.002	-0.016
	P	0.164	0.118	0.325	0.114	0.425	0.985	0.833
Cognitive flexibility	R	0093	0.140	0.046	0.084	0.099	0.035	0.027
	P	0.227	0.050	0.549	0.278	0.197	0.654	0.728

Table 6. Significance of differences p between three (for individual APOE gene polymorphism) correlations coefficients between cognitive functions (standardized results), and BMI and lipid levels in postmenopausal women examined

Cognitive functions	BMI (kg/m²)	CHOL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	LDL (mg/dl)	LDL/HDL	CHOL/HDL
NCI	0.134	0.750	0.631	0.911	0.587	0.423	0.442
Memory	0.508	0.094	0.638	0.961	0.168	0.536	0.655
Verbal memory	0.132	0.371	0.883	0.949	0.360	0.342	0.377
Visual memory	0.914	0.244	0.404	0.926	0.505	0.993	0.940
Processing speed	0.049	0.218	0.101	0.512	0.242	0.050	0.049
Cognitive functioning	0.199	0.939	0.521	0.867	0.810	0.546	0.577
Psychomotor speed	0.246	0.503	0.561	0.920	0.602	0.995	0.979
Reaction time	0.540	0.244	0.178	0.723	0.109	0.030	0.034
Complex attention	0.275	0.958	0.766	0.795	0.905	0.609	0.668
Cognitive flexibility	0.215	0.968	0.551	0.873	9.842	0.544	0.558

gene polymorphism on the correlations between cognitive functions, the BMI and lipid levels was examined using the model of covariance analysis (Tab. 6). Cognitive function was an explained variable (standardized results), and the explaining variables were: APOE gene polymorphism (3 categories: APOE2/3, APOE3/3, APOE3/4 or 4/4) and the level of lipids l (in natural units). An insignificance of the interaction was tested between APOE gene polymorphism and lipid level, i.e. the equality of three correlation coefficients between cognitive function and lipid for each from the three groups of APOE gene polymorphism. 70 such models of covariance analysis (10 cognitive functions * 7 lipids) were assessed. The significance level was set at p = 0.05.

RESULTS

170 postmenopausal women were examined. Table 1 presents their characteristics. In the study group, 31 women (18.2%) were carriers of APOE 2/3, 104 (61.2%) were carriers of APOE 3/3, and 35 (20.6%) were carriers of APOE 3/4 or 4/4. The mean age of women in the study was 56.4 ± 3.5 years. The mean BMI value was 26.5 ± 4.1 kg/m², three women (1.76%) were underweight (BMI<18.5 kg/m²), 62 women (36.47%) had normal body weight (18.5<BMI<25), 71 women (41.76%) were overweight (25<BMI<30), and 34 women (20.00%) were obese (BMI>30). The survey showed that in every third woman, body weight did not change after menopause, in 61% of the patients examined it increased, and in 6.5% – decreased. In the postmenopausal women examined, age, BMI, and change in body weight did not significantly depend on APOE gene polymorphism (p>0.05).

Table 2 presents the compilation of the results of analysis of lipid profile in the group of patients examined. Levels of total cholesterol, HDL and LDL cholesterols, as well as LDL/HDL and CHOL/HDL ratios, significantly depended on APOE gene polymorphism in the postmenopausal women examined (p>0.05). The mean value of total cholesterol was 228.3±44.0 mg/dl, HDL cholesterol 54.4±12.5 mg/dl, LDL cholesterol 144.4±45.5 mg/dl, and these mean values remained within normal values. In the group examined, 84% of women had total cholesterol above normal value (CHOL>191), 76.5% of women had LDL above normal (LDL>115), and 80% had HDL below normal (HDL<64). As many as 108 (63.5%) women in the study had abnormal total cholesterol – HDL and LDL – simultaneously. The mean values of LDL/HDL and CHOL/HDL ratios were 2.84±1.17 and 4.42±1.34, respectively. The mean LDL/HDL was close to the upper limit of the normal value, while mean CHOL/HDL was borderline. Normal LDL/HDL (<3) was observed in 58.24% of the women examined, LDL/HDL was borderline (3–4) in 27%, whereas highly risky (>4) in 15%. Normal CHOL/HDL (<4) was noted in 44.12% of women, CHOL/HDL on the borderline (4–5) in 25%, while highly risky (>5) in 31%.

The level of triglycerides significantly depended on APOE gene polymorphism possessed by patients (p=0.049). The lowest level of triglycerides was observed among the carriers of APOE 3/4 or 4/4 (mean 124.5 mg/dl), significantly higher in the carriers of APOE 3/3 and 2/3 (mean approximately 150 mg/dl). Normal triglyceride level was found in approximately three-quarters of the patients with APOE 3/4 or 4/4, or more rarely (in 55% patients) with APOE 3/3 and 2/3.

Analysis of cognitive functions according to the three groups of APOE gene polymorphism showed that in postmenopausal women three of these functions: executive functioning, psychomotor speed and cognitive flexibility (Tab. 3), significantly depended on the polymorphism of this gene (p<0.05). Patients possessing allele 2/3 obtained the best results with respect to the above-mentioned functions (mean values were approximately 90 scores, and signified the

assessment of these functions as between average and low average). Carriers of allele 3/3 obtained results concerning these three functions lower by approximately 10 scores than women with APOE 2/3, which indicates the evaluation of these functions between low and low average. Women with APOE 3/4 or 4/4 obtained results with respect to executive functioning and cognitive flexibility lower by the subsequent approximately 10 scores, compared to women with APOE 3/3 (i.e. evaluation between low and very low), while the results concerning their psychomotor speed did not significantly differ from the results of women with APOE 3/3.

Results pertaining to NCI and the remaining six cognitive functions – memory, verbal memory, visual memory, processing speed, reaction time and complex attention – significantly depended on APOE gene polymorphism ($p<0.05$).

It was confirmed that NCI and the following six cognitive functions: memory, processing speed, executive functioning, psychomotor speed, complex attention and cognitive flexibility significantly depended on changes of body weight after menopause ($p<0.05$) (Tab. 4). Women whose body weight decreased after menopause obtained significantly lower results in NCI and the six above-mentioned cognitive functions, compared to those whose body weight after menopause increased or remained unchanged. Mean results in NCI and the four cognitive functions – processing speed, executive functioning, complex attention and cognitive flexibility – in women who lost weight after menopause were from 60 – 67 scores, and evidenced very low evaluations in NCI and the indicated cognitive functions, while in the remaining women, mean values were from 80 – 92 scores, i.e. evaluations as average or low average.

The results concerning the following three cognitive functions – verbal memory, visual memory and reaction time – among the women examined did not significantly depend on change in body weight after menopause ($p>0.05$).

While analyzing correlations between cognitive functions and the BMI and lipid levels in postmenopausal women (Tab. 5), significantly positive correlations were observed between the results concerning visual memory and the BMI ($r=0.192$; $p=0.012$), and between the results pertaining to cognitive flexibility and total cholesterol ($r=0.140$; $p=0.050$). However, no significant correlations were confirmed between the remaining cognitive functions and the BMI, and the level of the remaining lipids in the total group in the study ($p>0.05$).

Table 6 presents the selected results of analysis of variance performed between cognitive functions and the BMI and lipid levels in the postmenopausal women examined, according to APOE gene polymorphism. According to APOE gene polymorphism, significant differences were found between LDL/HDL and CHOL/HDL ratios and results concerning processing speed and reaction time, as well as between the BMI and processing speed in the postmenopausal women examined ($p\leq0.05$). Figure 1 presents the correlations between cognitive functions and BMI and lipid level, which significantly differed according to APOE gene polymorphism. Significant positive correlations were observed between LDL/HDL and CHOL/HDL ratios, and results obtained in processing speed and reaction time in the group of women with APOE 2/3, while in the remaining two groups of women (with APOE 3/3 and APOE 4), no significant correlations between these variables were noted. In addition, a significant positive correlation was found between the BMI and results with respect to processing speed in the group of women with APOE 4, whereas in the remaining two groups of women (with APOE 2/3 and APOE 3/3), no significant correlations were observed between these variables.

No significant effect of APOE gene polymorphism on correlations between NCI and the remaining cognitive functions and levels of the remaining lipids was confirmed in the postmenopausal women in the study ($p>0.05$).

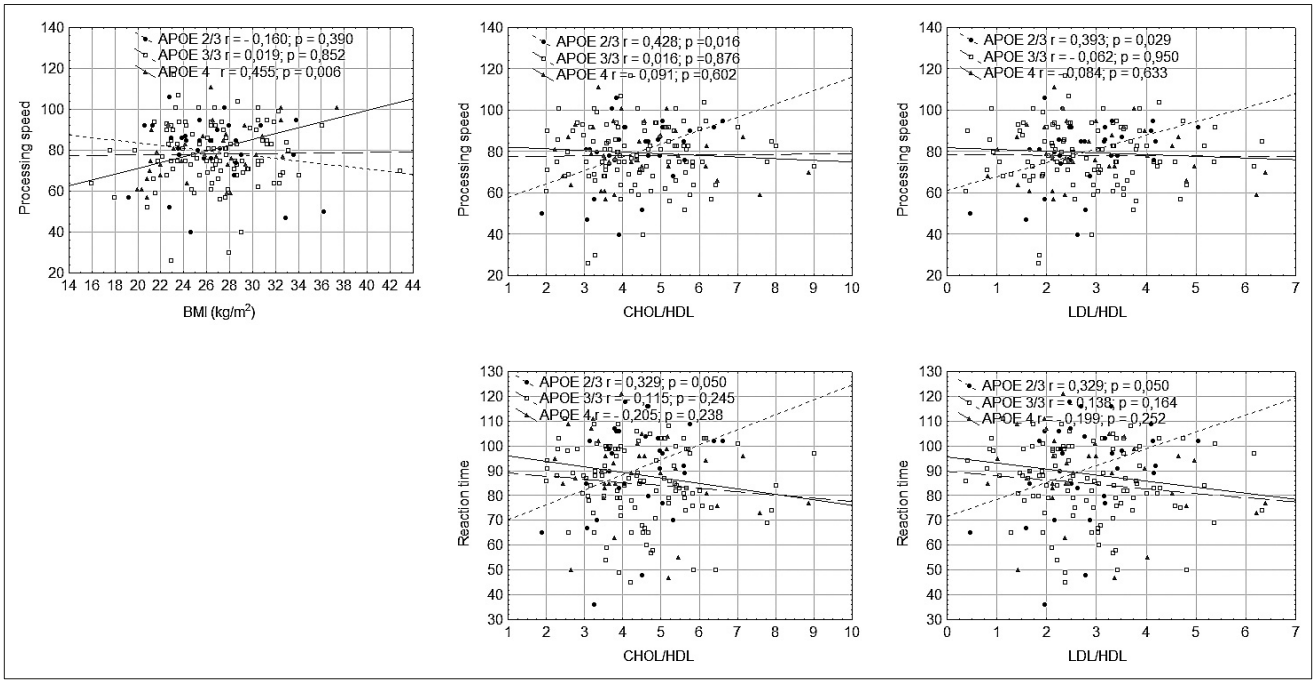

Figure 1. Correlations between cognitive functions (standardized results), and BMI and lipid levels in postmenopausal women in the study according to APOE gene polymorphism

DISCUSSION

Considering the fact that the pathological process may begin several years before cognitive problems are first observed [18], the detection of an elevated risk as early as possible may bring about new possibilities in the treatment and prophylaxis of cognitive disorders. Despite the fact that at the present stage of research, APOE gene polymorphism is poorly specific, it may be a very important supplementation to the classification of female patients at peri- and postmenopausal period into the group of transitory form of mild cognitive disorders, in whom prophylaxis is important, and into the group of patients in whom cognitive disorders are the first symptoms of developing dementia and who require treatment.

In the presented study conducted in a group of postmenopausal women, similar to other studies [8, 9, 10, 11, 12, 13, 14], the effect of carrying APOE4 is a higher risk of development of cognitive disorders was confirmed. It was found that only the level of TG significantly depended on APOE gene polymorphism possessed by the patients. Women who were carriers of APOE 3/4 or 4/4 had the lowest TG results, whereas the carriers of APOE 3/3 and 2/3 had significantly higher results. The levels of the remaining lipids and LDL/HDL and CHOL/HDL ratios did not significantly depend on APOE gene polymorphism. Nevertheless, significant differences according to APOE gene polymorphism were observed in correlations between LDL/HDL and CHOL/HDL ratios, and results concerning processing speed and reaction time.

In the literature, there is no unequivocal evidence for unfavourable effects of abnormal lipids values on the level of cognitive functions in carriers of individual APOE polymorphisms. There are studies which do not confirm any significant relationship between carrying APOE gene polymorphism and the level of various lipids which might participate in the development of vascular and dementia changes [19]. Studies by Bennet et al. showed a linear relationship between APOE gene and the level of LDL cholesterol. In those studies, carriers of APOE4 had higher results with respect to LDL cholesterol, while carriers of the genotype APOE2 – the lowest [20]. In the studies conducted among 305 women in Korea, a negative relationship was found between apoE2 and the level of HDL cholesterol, whereas there was a positive relationship between APOE4 and the level of LDL cholesterol [21]. In the studies by Sertic et al., a significant relationship was observed between APOE and hypercholesterolaemia. Patients with APOE 2/3 had a lower cholesterol level, while those with APOE 3/4 – a higher level [22]. Interesting information may be found in studies by Katerina et al., in which it was discovered that APOE isoforms and menopause may act as strong modulators of the level of HDL cholesterol [23].

In the NEDICES study (Neurological Diseases in Central Spain Study), which covered 1,949 individuals aged at least 65, it was observed that both obesity and overweight were related with the lowest results obtained in the parameters describing intelligence, memory, verbal fluency and psychomotor efficacy. According to Benito-León et al., there is a relationship between obesity and the deterioration of cognitive functions [24]. However, in the presented study it was confirmed that the lowest results with respect to memory, processing speed, executive functioning, psychomotor speed, complex attention and cognitive flexibility were obtained by women whose body weight decreased after menopause, compared to those whose weight after menopause increased or remained unchanged. Similarly, in the studies by Struman et al., no considerable cognitive deficits were noted in both obese and overweight patients. After consideration of gender, race, age and education level, a higher BMI was associated with lower impairment of cognitive functions during observations. In addition, similar to the presented study, the deepening of cognitive deficits during the study was noted in underweight patients [25]. However, researchers from Northwestern University's Feinberg School of Medicine analyzed data collected in the study Women's Health Initiative in a group of women aged at least 65. In this study, the BMI was compiled with information concerning cognitive functions, and confirmed that the higher the BMI, the lower the results with respect to cognitive functions. The researchers proposed a theory that cardiovascular problems and inflammatory states caused by obesity may cause damage to the brain which, in consequence, lead to dementia. However, further analysis showed that the relationship between the BMI and cognitive skills is more complicated. Among women with the highest waist circumference to hip ratio the results of cognitive tests increased with the BMI. This may suggest that the fatty tissue in the abdominal cavity contributes to the production of oestrogen – the hormone which may increase the efficacy of the brain, and in this way eliminate the negative effect of general obesity on cognitive functions [14].

Despite studies showing that APOE isoforms are related with an increase in the Body Mass Index in the sequence: apoE2<apoE3<apoE4, based on the results of the presented study, it is not possible to unequivocally state whether the carrier status of individual APOE gene polymorphisms affects the relationships between lipidogram, BMI, and changes of body weight and cognitive functions in postmenopausal women.

CONCLUSIONS

1) In the postmenopausal women examined, the carrier state of APOE gene polymorphism was associated with the level of triglycerides and the results concerning three cognitive functions: executive functioning, psychomotor speed, and cognitive flexibility.
2) Loss of body weight in postmenopausal women was related with lower results in NCI and the majority of cognitive functions.
3) The results concerning cognitive functions in postmenopausal women in the study were not significantly related with lipid profile.
4) Significant differences were observed according to APOE gene polymorphism in correlations between LDL/HDL and CHOL/HDL ratios, and results in the processing speed and reaction time, as well as between the BMI and results in processing speed in the postmenopausal women examined.

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