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THE ASSOCIATION BETWEEN CHOLESTEROL LEVELS AND BRACHIAL/AORTIC AUGMENTATION INDEX VERSUS COGNITIVE STATUS IN PATIENTS WITH CARDIOVASCULAR RISK FACTORS

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Abstract - Cardiovascular pathology appears to have a major impact in cognitive decline, and early identification and correction of cardiovascular morbidity could have a major protective impact on cognitive functioning. However, it is not clear how the risk factors for vascular disease can also be risk factors for a general cognitive decline. Regarding cholesterol, its implications in cognitive decline are not very well understood, considering that a high level of cholesterol has been associated with both an increased and decreased risk of dementia. In the present context, we decided to study correlations between cholesterol concentration and the various subdomains of some main psychometric tests, such as MMSE (Mini-Mental State Examination) and MoCA (The Montreal Cognitive Assessment), as well as some measurements for systemic arterial stiffness (brachial and aortic augmentation index) and how they correlate with the aforementioned psychometric parameters. Our results provide additional evidence for a correlation between cholesterol levels and cognitive subdomains (with special focus on orientation, attention, recent memory and long-term memory). Additionally, a significant correlation was found between the brachial and aortic augmentation index and the results of both MMSE and MOCA tests.

Key words: Cholesterol, cognitive deficits, brachial and aortic augmentation index

INTRODUCTION

Cognitive deficits generally increase with aging. Also, the presence of vascular risk factors such as hypertension, cholesterol, diabetes mellitus or the presence of heart diseases may increase the risk of developing Alzheimer's disease (AD) (McCullagh et al., 2001, Schneider et al., 2004, Luchsinger et al., 2005, Ciobica et al., 2011c). In this way, cardiovascular pathology appears to have a major impact in cognitive decline, and an early identification and correction of cardiovascular morbidity could have a major protective impact on cognitive functioning (Ciobica et al., 2009, 2011a, b). However, it is not very clear how the risk factors for vascular disease can also be risk factors for a general cognitive decline.

We previously studied the possible connections between blood pressure and body mass index to the cognitive functions in patients with cardiovascular risk factors (Joacabine et al., 2011a, b). It is also believed that hypertension and hypercholesterolemia increase the risk of dementia by inducing atherosclerosis and impairing blood flow, but they may also directly induce the neurodegeneration of Alzheimer's disease (Kivipelto et al., 2001). Regarding cholesterol, it is generally accepted that high total choles-

terol is a common marker of cardiovascular and cerebrovascular pathology. However, its implications in cognitive decline are not very well understood, considering that a high level of cholesterol has been associated with both an increased and decreased risk of dementia (Notkola et al., 1998, Kivipelto et al., 2002, Solomon et al., 2007, Ciobica et al., 2011).

We decided to study the degree of cognitive decline in selected patients with reported cardiovascular problems. Moreover, in the present paper we will extensively present the correlations between cholesterol concentration and the various subdomains of some of the main psychometric tests, like MMSE (Mini-Mental State Examination) and MoCA (The Montreal Cognitive Assessment). Additionally, considering the importance of cholesterol in increasing vascular resistance and rigidity, in the present paper we will determine some indices for peripheral vascular resistance (brachial and aortic augmentation index, which are a measure for the systemic arterial stiffness (Fantin et al., 2007)) and how they correlate with the aforementioned psychometric parameters.

MATERIALS AND METHODS

This study (n=95 patients) consisted of 80 patients (46 females and 34 males; age: 61.2 years±4.7), with reported cardiovascular problems, and 15 healthy age-matched controls (9 females and 6 males; age: 59.5 years±5.8). Patients were recruited from the University Hospital of Psychiatry "Socola", Iaşi, Romania.

Exclusion criteria were represented by acute comorbidities, chronic unstable diseases as well as patients with other medical conditions that could lead to cognitive deficits apart from cardiovascular and metabolic dysfunction.

Healthy control subjects had major psychiatric disorders excluded based on history taking and psychiatric examination, according to the DSM-IV checklist. The demographic data of the controls were chosen in order to match the patients with cardiovascular problems.

Cognitive testing was performed in the morning, between 10-12 a. m. Blood samples were obtained in the morning before breakfast. Blood was allowed to clot and was centrifuged immediately (Padurariu et al., 2010 a, b). Sera were aliquoted into Eppendorf tubes and stored at -80°C until determination of serum total cholesterol concentrations, which was performed in the hospital central laboratory.

The augmentation index is an indirect measure of arterial stiffness. It is calculated as augmentation pressure divided by pulse pressure ×100 to give a percentage. With an increase in stiffness, there is a faster propagation of the forward pulse wave as well as a more rapid reflected wave (O'Rourke et al., 2008). Measurement of the brachial and aortic augmentation index was performed by using a TensioMed Arteriograph (Budapest, Hungary). All readings recorded met the manufacturer's quality control standards integrated into the software package.

The study was conducted according to provisions of the Helsinki Declaration and all the patients signed consent for participation in this study.

Statistical analysis

The results for the cholesterol levels and brachial and aortic augmentation index were analyzed using one-way analysis of variance (one-way ANOVA). All results are expressed as mean ± SEM. F values for which $p<0.05$ were regarded as statistically significant (Hritcu et al., 2011, Hogas et al., 2011, Padurariu et al., 2012). In addition, Pearson's correlation coefficient was used to evaluate the connection between the cholesterol levels or the brachial and aortic augmentation index values versus various subdomains of certain psychometric tests such as MMSE and MOCA.

RESULTS

Our initial analysis included cholesterol levels. As expected, we observed a significant increase ($F(1.93)=19$, $p<0.001$) in cholesterol concentration

in patients with reported cardiovascular problems, compared to our control group (Fig. 1).

More importantly, when we analyzed the connections between the cholesterol levels and the results from the MMSE and MOCA tests, we found significant negative correlations for cholesterol vs. MMSE (n=95, r=-0.308, p= 0.002) (Fig. 2) and for cholesterol vs. MOCA (n=95, r=-0,366, p<0.0001) (Fig. 3).

Additionally, we found significant negative correlations between the values of the cholesterol level and some of the subdomains of both MMSE: cholesterol vs. orientation (n=95, r=-0.195, p<0.047) (Fig. 4A), cholesterol vs. attention (n=95, r=-0.406, p< 0.0001) (Fig. 4C), cholesterol vs. recent memory (n=95, r=-0.305, p= 0.003) (Fig. 4D) and MOCA tests: cholesterol vs. long-term memory (n=95, r= -0.198, p= 0.048) (Fig. 5F).

However, in the case of some subdomains of the MMSE test, we could not find any significant correlations as in the case of cholesterol vs. short-term memory (n=95, r=-0.094, p=0.364) (Fig. 4B), cholesterol vs. language (n=95, r=-0.094 , p= 0.367) (Fig. 4E) and cholesterol vs. executive functions (n=95, r= -0.01 , p=0.925) (Fig. 4F). Also, we did not observe any correlations between cholesterol values and the rest of the cognitive subdomains of the MOCA test: cholesterol vs. visuospatial/executive functions (n=95, r=-0.039, p= 0.711) (Fig. 5A), cholesterol vs. naming (n=95, r=-0.046, p=0.657) (Fig. 5B), cholesterol vs. attention (n=95, r=-0.156, p=0.132) (Fig. 5C), cholesterol vs. language (n=95, r=-0.105, p=0.315) (Fig. 5D), cholesterol vs. abstractization (n=95, r=-0.084, p=0.419) (Fig. 5E) and cholesterol vs. orientation (n=95, r=-0,077, p<0,456) (Fig. 5G).

Regarding the values of the augmentation index, we demonstrated a significant decrease of both the brachial (F(1.93)=11, p=0.042) (Fig. 6), as well as aortic augmentation index (F(1.93)=19, p=0.03) (Fig. 7) in the patients with reported cardiovascular problems, as compared to the control group.

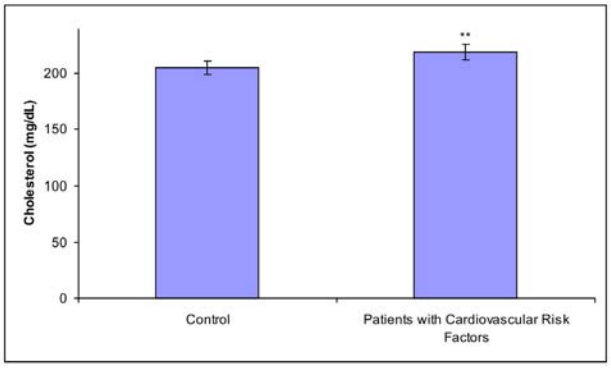

Fig. 1. Cholesterol concentration in cardiovascular patients and controls. The values are mean ± S.E.M. (n=80 for cardiovascular patients and n=15 per control group). ** p < 0,001.

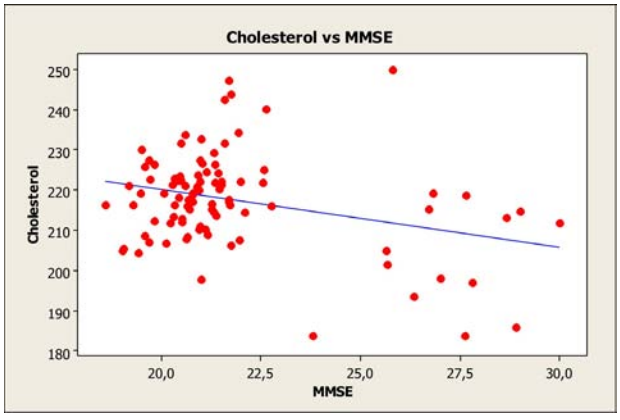

Fig. 2. Correlations between cholesterol levels and MMSE (n=95, r= -0,308, p= 0,002)

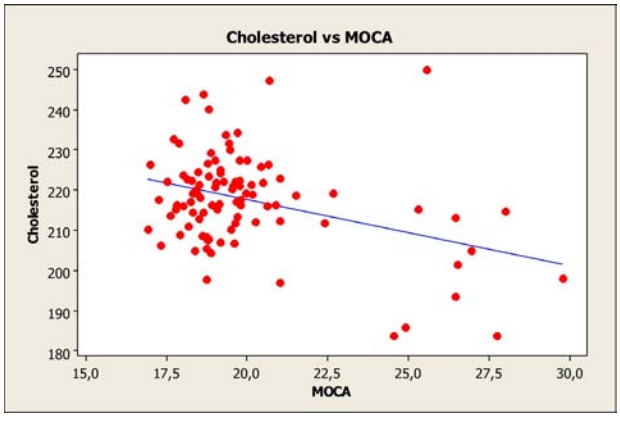

Fig. 3. Correlations between cholesterol levels and MOCA test. (n=95, r= -0,366, p< 0,0001).

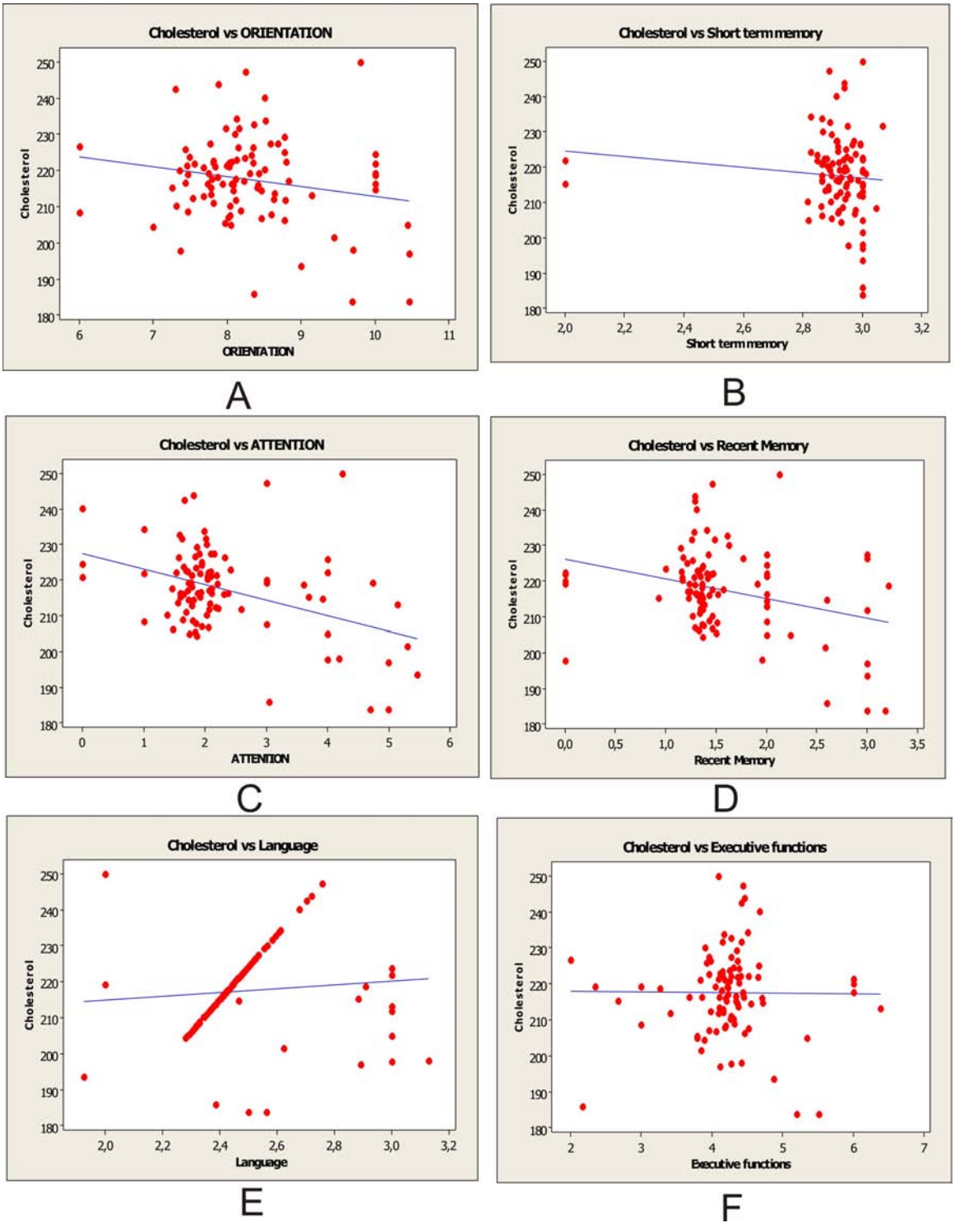

Fig. 4. Correlations between cholesterol levels and the subdomains of MMSE.

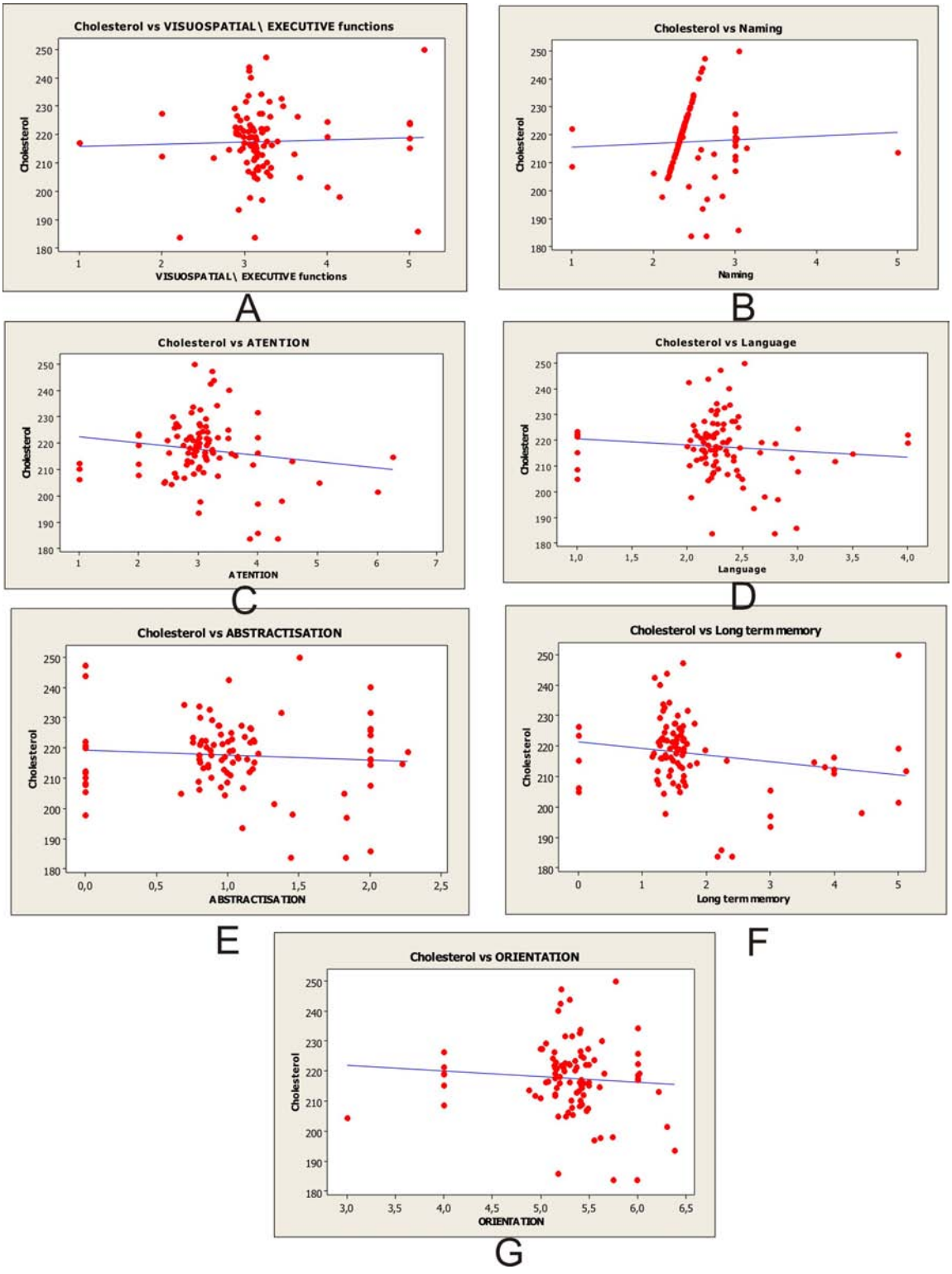

Fig. 5. Correlations between cholesterol levels and the subdomains of MOCA test.

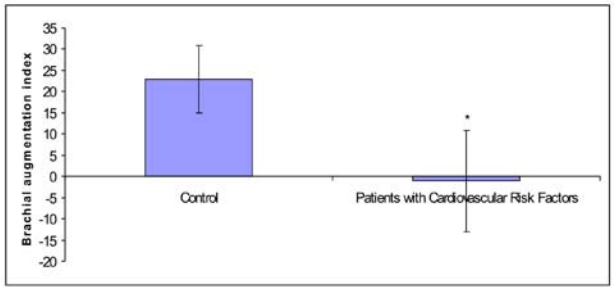

Fig. 6. Brachial augmentation index in cardiovascular patients and controls. The values are mean ± S.E.M. (n=80 for cardiovascular patients and n=15 per control group). * p = 0,042.

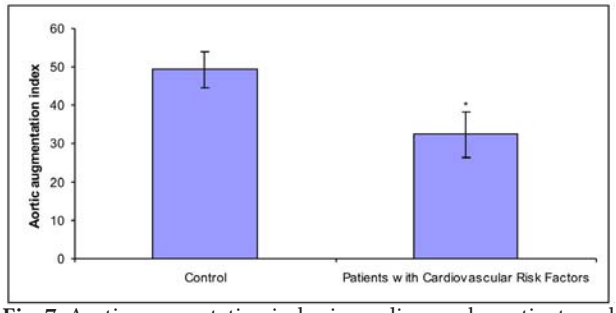

Fig. 7. Aortic augmentation index in cardiovascular patients and controls. The values are mean ± S.E.M. (n=80 for cardiovascular patients and n=15 per control group). * p = 0,03.

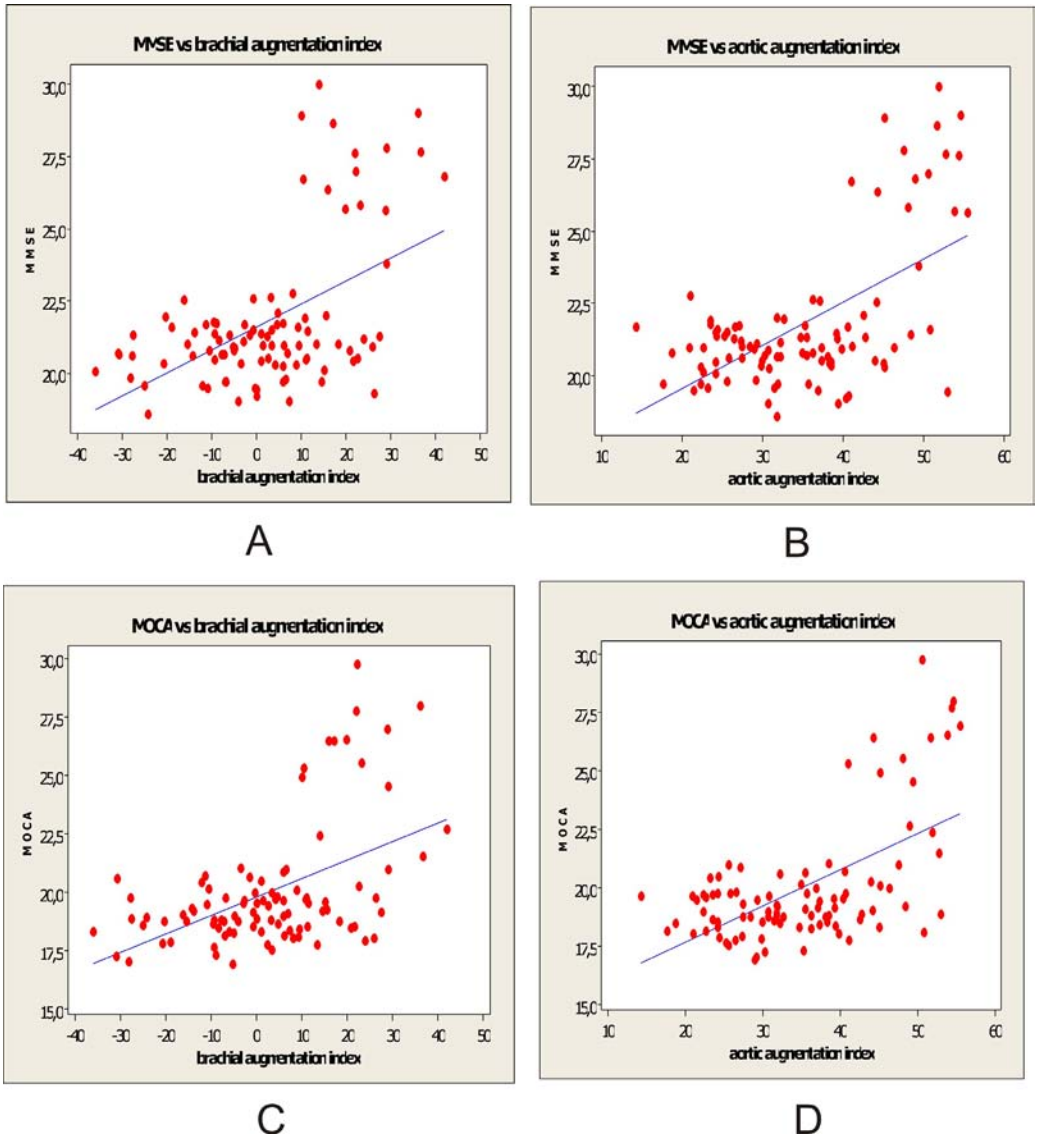

Fig. 8. Correlations between brachial/aortic augmentation index and the MMSE/MOCA tests.

More importantly, when we analyzed the connections between the cholesterol levels and the results from MMSE and MOCA tests, we found significant correlations between MMSE vs. brachial augmentation index (n=95, r=0.517, p<0.0001) (Fig. 8A), as well as for MMSE vs. aortic augmentation index (n=95, r= 0.591, p<0.0001) (Fig. 8B). Also, significant correlations were reported between MOCA vs. brachial augmentation index (n=95, r=0.493, p<0.0001) (Fig. 8C), as well as for MOCA vs. aortic augmentation index (n=95, r=0.589, p< 0.0001) (Fig. 8D).

DISCUSSION

Our results provide additional evidence for a correlation between cholesterol levels and cognitive deficits (Notkola et al., 1998, Kivipelto et al., 2002, Solomon et al., 2007, Ciobica et al., 2011), expressed in our study by the specific scores of the MMSE and MOCA tests. Moreover, we demonstrated a series of significant correlations between cholesterol values and some of the subdomains from the MMSE and MOCA tests. Additionally, a significant correlation was found between some measurements of the systemic arterial stiffness (brachial and aortic augmentation index) and the results of both MMSE and MOCA tests.

As previously mentioned, a high level of cholesterol was associated with both an increased and decreased risk of dementia. It seems that this varies mainly with the age of the studied patients. In this way, a decreased level of serum cholesterol was demonstrated to have a positive correlation with cognitive regression in late-life (Solomon et al., 2007), while there is also evidence that cholesterol is starting to decrease several years before the onset of dementia, and this could be used as a marker for the risk of AD (Mielke et al., 2005). In addition, other studies identified cholesterol as a risk factor for AD when this was found in middle-aged patients (Notkola et al., 1998, Kivipelto et al., 2002, Solomon et al., 2007).

Regarding the augmentation index, this is considered to be a measure of systemic arterial stiffness (Fantin et al., 2007, O'Rourke et al., 2008). Previous studies have demonstrated an association between the augmentation index and risk factors of cardiovascular disease (Janner et al., 2011). In addition, there are many gaps in this area of research, especially regarding the age and gender differences of the observed associations (Janner et al., 2011). However, in our study we were more interested to find the connections between the brachial and aortic augmentation index and the results of some specific cognitive tests, such as MMSE and MOCA. The strong connections that were demonstrated between these aspects can be also applied at the central level and further studies in this area seem warranted. Interestingly enough, the brachial and aortic augmentation index exhibited much stronger connections with the cognitive tests, in comparison with cholesterol, which might suggest their possible superiority as markers for the cognitive decline.

CONCLUSIONS

The present study provides additional evidence for the existence of a correlation between cholesterol levels and cognitive deficits (with special focus on orientation, attention, recent memory and long-term memory). Moreover, we demonstrated significant connections between the measurements of systemic arterial stiffness, such as the brachial and aortic augmentation index, and the results of the specific cognitive tests (MMSE and MOCA).

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