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Correlation of blood pressure with cognitive function tests' results in older people. Preliminary results of the Train Your Brain Study

Korelacja poziomu ciśnienia tętniczego z wynikami testów funkcji poznawczych u osób starszych. Wstępne wyniki badań Trenuj Swój Mózg

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Abstract

Introduction. *In healthy organism, BP level in the periphery should not influence on the effectiveness of regulation of intracranial blood pressure (BP) and hemodynamics. However, independence of these mechanisms could be disrupted during aging. Some hypothetical mechanisms describe how prolonged hypertension could affect cognitive functioning deterioration in older people. However, there is little evidence, which would confirm such coexistence between these variables.* ***Aim.*** *The aim of this study is to assess the level of correlation between results of cognitive tests with blood pressure level.* ***Material and methods.*** *In these preliminary studies 128 patients (21 men, mean age: 68.80, age range 58-88) were examined. Cognitive functioning was assessed by Mini–Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Trail Making Test Part B (TMT B). Blood pressure: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Pulse Pressure (PP) were examined.* ***Results.*** *DBP, SBP and MAP were significantly and negatively correlated with verbal fluency subtest of MoCA ($r = -0.1945$, $-0,2414$ and -0.2373), respectively. In group comparison, normotensive participants pronounced approximately 1.8 words more than their hypertensive counterparts in Verbal Fluency subtest. However, other results were not statistically significant ($p > 0.05$).* ***Conclusions.*** *In these preliminary studies we examined correlation of blood pressure with cognitive function tests. Only verbal fluency subtest of MoCA results were significantly and negatively correlated with DBP, SBP and MAP. Longitudinal studies on larger samples are needed to estimate the level and direction of hypertension relations with cognitive functioning in older people. Gerontol Pol 2017; 25: 53-59)*

Key words: *Blood pressure, cognitive functioning, older people, Trail Making Test part B, MoCA, MMSE*

Streszczenie

Wstęp. *W zdrowym organizmie poziom ciśnienia tętniczego na obwodzie nie powinien wpływać na efektywność regulacji ciśnienia i hemodynamiki wewnątrzczaszkowej. Jednak niezależność tych mechanizmów może zostać zaburzona w procesie starzenia się. Niektóre hipotetyczne mechanizmy opisują w jaki sposób długotrwałe nadciśnienie może wpłynąć na*

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zaburzenie funkcji poznawczych u osób starszych. Jednak niewiele jest danych, które mogłyby potwierdzić współwystępowanie tych zmiennych. ***Cel.*** *Celem niniejszej pracy jest ocena poziomu korelacji pomiędzy wynikami testów poznawczych a ciśnieniem tętniczym krwi.* ***Materiał i metody.*** *W niniejszych, wstępnych badaniach 128 pacjentów zostało przebadanych (21 mężczyzn, średnia wieku: 68,80, przedział wiekowy 58-88). Funkcjonowanie poznawcze oceniano za pomocą testów: Mini–Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) i Test Łączenia Punktów Część B (TMT B). Zmierzone zostało skurczowe (SBP) i rozkurczowe ciśnienie tętnicze (DBP), średnie ciśnienie tętnicze (MAP) oraz ciśnienie tętna (PP).* ***Wyniki.*** *DBP, SBP i MAP były istotnie ujemnie skorelowane z podtestem MoCA-Fluencji werbalnej (odpowiednio: r = -0,1945, -0,2414 -0,2373). Porównując grupy, uczestnicy z prawidłowym ciśnieniem wymawiali około 1,8 słowa więcej, niż ich odpowiednicy z nadciśnieniem tętniczym. Jednakże, reszta wyników nie była statystycznie znacząca (p > 0,05).* ***Wnioski.*** *W niniejszych, wstępnych badaniach oceniono stopień korelacji ciśnienia krwi z wynikami testów funkcji poznawczych. Jedynie wyniki Fluencji werbalnej - podtestu MoCA - były istotnie, ujemnie skorelowane z DBP, SBP i MAP. Potrzebne są podłużne badania na większej grupie osób, aby oszacować poziom i kierunek korelacji nadciśnienia z poziomem funkcjonowania poznawczego u osób starszych. Gerontol Pol 2017; 25: 53-59)*

Słowa kluczowe: *ciśnienie tętnicze, funkcjonowanie poznawcze, starsze osoby, Test Łączenia Punktów Część B, MoCA, MMSE*

Introduction

Nowadays, more and more attention is focused on relationship of cardiovascular system and cognitive functioning. In a normal, healthy organism an effective regulation of intracranial blood pressure (BP) and hemodynamics should not be influenced by the peripheral BP standardly measured by sphygmomanometer on upper arm. However, this 'classic' view on BP auto-regulation comes from older studies, before implementation of methods such as a continuous, beat-to-beat BP measurement or transcranial Doppler which allows to directly measure cerebral blood flow [1]. Moreover, as review from 2013 showed, [1] intracranial BP is not so constant, as it was believed to be, contrary, it appears that intracranial BP tends to fluctuate. Noteworthy, several brain autoregulation mechanisms are classically described in terms of 'homeostasis' what could be misleading; 'stasis' might not reflects well the dynamics of intracranial hemodynamic and pressure regulation processes.

During aging, several pathological processes could contribute to homeostasis disruption. Interestingly, longitudinal studies [2] showed, that older patients with chronic hypertension (defined as > 140/90 mmHg) had lower regional cerebral blood flow measured by resting-state PET scans. Measurements were done several times during 7 years; comparing results from year 1 to year 7, chronic hypertensive patients showed diminished regional cerebral flow in inferior frontal, precentral, middle temporal, parahippocampal, and fusiform gyri [2]. These regions were identified countless times in functional MRI examinations as active while performing cognitive tests. Therefore, many epidemiological researches from last decades had examined and showed associations between level of blood pressure and cognitive performance [3-8].

One of so-called Geriatric Giants is dementia. Low effectiveness in word retrieval during verbal fluency may be one of the initial signs of dementia [9]. Studies from

2015, incorporating 1052 patients 51 years old and over without diagnosed dementia, noted an increased functional hemodynamics in right prefrontal and bilateral parietal cortex, and decreased in bilateral inferior frontal junction during phonological fluency using functional near-infrared spectroscopy. Despite no statistically significant results, some factors, inter alia, hypertension was correlated with decreased blood flow in left inferior frontal junction during phonological fluency [10]. Underlying mechanisms, in which BP is associated with cognitive functions could be various. To explain it further, researchers used MRI to examine brain geometry of 40 participants with hypertension-diagnosis and their 40 sex and ethnicity-matched normotensive controls [11]. Results showed that participants with hypertension had diminished area of gray matter in prefrontal cortex and underlying white matter volumes and increased frontal white-matter hyperintensities occurrence, which potentially could be associated with continuous exposure on hypertension. Moreover, other studies using structural MRI [12] showed that elevated SBP is a predictor of diminished volume of several grey matter structures, inter alia, supplementary motor area. In male participants, diminished volume in this area predicted worse results in Trail Making Part B Test and in Four-word Short-term Memory Test.

Most studies with regard to BP in older patients are based on correlations, therefore results could not tell anything about the direction of influence. Considering above mentioned information, it is not the surprising, that several researches examined influence of the hypertension treatment on cognitive functioning. Results were conflicting, from improved cognitive functioning and lowered rate of vascular dementia occurrence [13,14], to

diminishing cognitive performance due to intervention [15,16]. However, in the case of the above-mentioned interventions some methodological problem could occur, namely: drugs, which actions is supposed to lower blood pressure could, in fact, influence also on cognitive functions. For example, Ca2+ antagonists have potential to improve cognitive performance not only in hypertensive but also in normotensive participants [13].

A review from 2009 [7] shows, that the results of correlation of BP with cognitive functioning is observed in studies in the manner of a traditional cross-sectional study and noted conflicting results: some of the relationships were positive, some negative as well as J- and U-shape nonlinear correlations were noted. On the other hand, longitudinal studies showed that increased BP is positively correlated with rate of cognitive decline. Results of only a few available randomized controlled trials indicate heterogeneous effects of BP lowering on cognitive function. Authors explain these conflicting results [7] by a yet-unknown and complicated nature of a biological mechanism in which chronic elevated or lowered blood pressure can influence on cognitive functioning.

Considering the above-mentioned issues, there is strong need for further development of this topic. However, due to the conflicting results, it would be necessary to examine a direct correlation of BP and cognitive functioning. Moderate or severe dementia seems to co-occur with lower BP values [3]. Interestingly, other studies [4] showed no correlation between BP and cognitive functioning; however, when data from follow-up (20 years) were included, average BP over 20 years was negatively correlated with cognitive performance [4]. Kuo [5] et al found positive correlation between SBP and relative risk of diminished performance in Trail Making Test Part B. The highest risk was established in group with the highest SBP (146-185 mmHg). However, BP and neuropsychological tests (Logical memory I & II, Visual reproduction I & II recall, Copy and discrimination tests) were not correlated [5].

Studies examined sixty hypertensive patients, ages 65 and older, control groups were composited of 30 normotensive participants [6]. Normotensive group outperformed hypertensive group in, inter alia, Trail Making Test part B [6]. In advanced stages of cognitive decline, this could be attributed as secondary phenomenon [17], probably due to pathological changes in functioning of medullary cardiovascular center. Therefore, in our studies, we made two analyses: one with all participants, and second with excluded patients with diagnosis of MCI or dementia.

Aim

The aim of this study is to assess the level of correlation between results of cognitive tests with blood pressure level.

Material and methods

Patients were enrolled into studies on base of regional radio and TV advertisements, during public health-promoting lectures, in Day Care Centers for the Elderly, and on various meeting-groups for older people. Assessment was conducted at Collegium Medicum University Hospital in Bydgoszcz, in Department and Clinic of Geriatrics and Department of Hygiene, Epidemiology and Ergonomics and was approved by the local ethics committee at the Collegium Medicum University (KB 340/2015). The first visit consisted of blood collection, neuropsychological, medical, social, economical, dietary and physiotherapy assessments, what together took three hours per one patient. Schedule of the examinations was arranged in a way to set blood collection, followed by neuropsychological assessment as first examinations.

In these preliminary studies 128 patients (21 men, mean age: 68.80, age range 58-88) were examined. Cognitive functioning was assessed with Mini–Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Trail Making Test Part B (TMT B). MMSE is a well-known 30-points questionnaire used in neuropsychological assessment, it measures orientation to time and place, immediate recall and short-term verbal memory, calculation, language, and construct ability. The higher score indicates better cognitive performance. We assumed 24 point as cut-off score for Mild Cognitive Impairment diagnosis. MMSE is characterized by rather worse specificity and sensitivity than MoCA, however, plenty of similar researches are based on this test, therefore, MMSE has been incorporated into studies.

The MoCA assesses several cognitive domains. It measures all main cognitive domains; namely visuospatial skills, short-term memory recall, executive functioning (examined by a mini-form of trail-making B task, phonemic fluency task and a two-item verbal abstraction task). Attention, and working memory as well as naming and other language skills were evaluated. In MoCA test result of two subtests (Verbal Fluency subtest and delayed recall of five nouns) were taken into account separately during analysis.

Trail Making Test part B is a fast-to-assess neuropsychological tool, which measures various skill from executive functioning domain: visuospatial skills, task swit-

ching and working memory to mention a few). We assumed > 26 score for MoCA as a cut-off score for Mild Cognitive Impairment (MCI) diagnosis. However, if patient had score 25 and lower in MoCA, but MMSE score was 28-30 points, the cognitive functioning of patient was described as normal. Blood pressure: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured on one followed by another upper limb. All of the examinations were done in doctor's office, while physician was casually dressed most often, to minimize possible influence of 'white-coat' effect [18]. Mean value for each patient's SBP and DBP from these two measurements were analyzed. Hypertension diagnosis was diagnosed based on SBP > 140 or DBP > 90. Moreover, Pulse Pressure (PP) PP=SBP-DBP as well as mean arterial pressure (MAP=DB+1/3(SBP-DBP) were calculated.

Correlation of above mentioned variables was measured with r-Pearson test. For group comparison (Mild Cognitive Impairment *vs.* cognitively intact) between differences in blood pressure scores independent-samples t-test was used. All statistical analyses were performed using statistical package (StatSoft, Inc. (2014). STATISTICA (data analysis software system), version 12. www.statsoft.com).

Results

Description of participants

Table I. Correlation of blood pressure with cognitive function tests results in older people

Characteristics (n1. n2)	Percentage/Mean (SD)
Age	68.80 (6.08)
BMI	26.94 (4.20)
Education years>14	41.4%
Worked/working as physical worker	18.75%
Still maintain a job position	17.96%
Hypertension diagnosis	45.31%
Current smokers	7.03%
SBP (n1=122)	140.94 (21.11)
DBP (n1=122)	83.77 (10.94)
TMT B (n1=116. n2=107)	125.61 (57.74)
MoCA (n1=128. n2=128)	23.89 (3.20)
MoCA Verbal Fluency (n1=127. n2=124)	12.86 (4.22)
MoCA Delayed Recall (n1=128. n2=128)	2.21 (1.61)
MMSE (n1=128. n2=128)	27.46 (2.26)
MCI diagnosed	36.71 %

Description of Participants (n = 128)
The *n* in circle brackets after tests name indicates number of participants before (n1) and after (n2) ignoring outliers

Participants age ranged from 58 to 88 years old. Mean Body Mass Index (BMI) in our study-group was calculated as 26.94. Our participants were well educated, their mean years of education is 14.12 (ranged 7-23 years). 24 of them were working in past, or still working as a physical employee, rest were white-collar workers or owner of a craft, service, entrepreneur or maintained other jobs. 23 participants still maintain a job position. There was 58 participants with diagnosed hypertension based on measurement in our study (SBP > 140 or DBP > 90). Moreover, there were 9 current smokers in this group. Mild Cognitive Impairment was diagnosed in 47 participants.

Cognitive functioning tests and blood pressure in all (normal + MCI)

Significant, moderate positive correlation between MoCA and MMSE results ($r = 0.45611$, $p < 0.05$), and weak positive correlation between MMSE and Verbal Fluency subtest of MoCA ($r = 0.2718$, $p = 0.05$) were observed. TMT B results correlated with MMSE and MoCA ($r = -0.4111$ and $r = -0.5616$, $p < 0.05$ respectively).

DBP, SBP and MAP were negatively correlated with Verbal Fluency subtest of MoCA ($r = -0.1945$, $p = 0.049$), ($r = -0.2414$, $p = 0{,}014$) and ($r = -0.2373$, $p = 0.016$), respectively. Pulse Pressure was slightly negatively correlated with Verbal Fluency subtest ($r = -0.1531$), however this result was not statistically significant ($p > 0.05$).

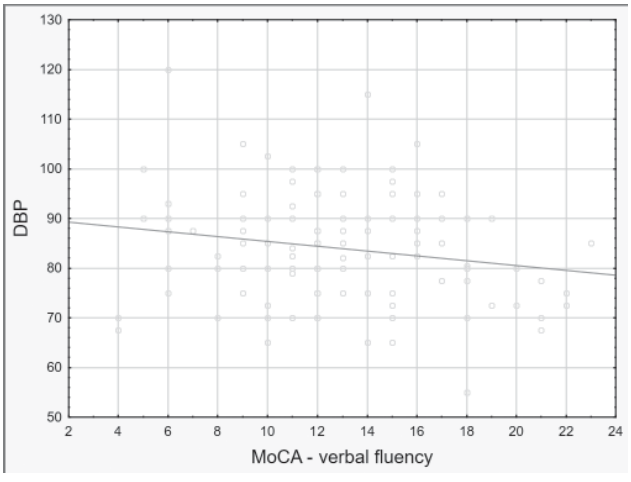

Figure 1. Correlation of blood pressure with cognitive function tests results in older people

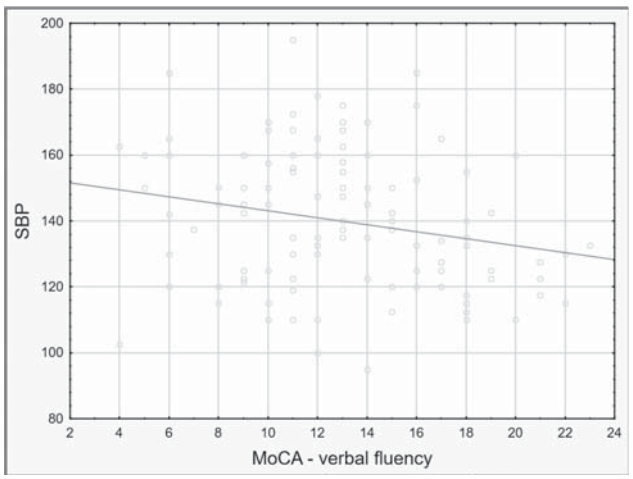

Figure 2. Correlation of blood pressure with cognitive function tests results in older people

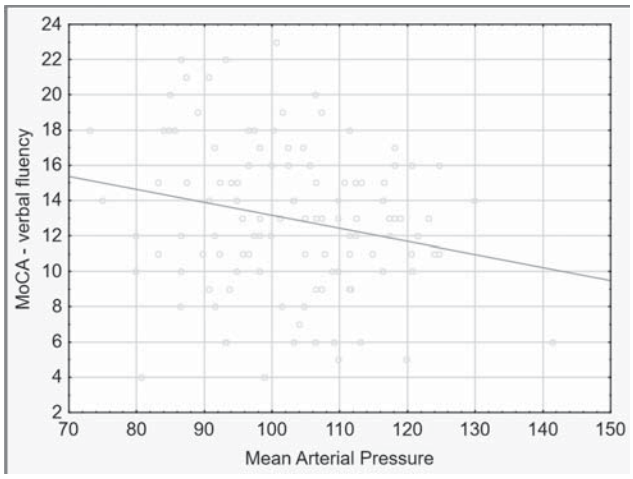

Figure 3. Correlation of blood pressure with cognitive function tests results in older people

Other correlations were statistically nonsignificant: SBP and DBP were slightly, positively correlated with MMSE (r = 0.0909, r = 0.0218), MoCA results were slightly negatively correlated with SBP and positively with DBP (r = -0.0613, r = 0.0280). TMT B results were positively correlated with SBP (r = 0.0602) and DBP (r = 0.0440).

Group comparison between normal and hypertensive group

Hypertension was diagnosed on basis of measurements by physician during examination at our studies. SBP > 140 or DBP > 90 was a criteria for hypertension. Based on these diagnoses, two groups: normotensive and hypertensive were separated. To examine differences between mean scores of cognitive functioning test, T test for independent variables was selected.

Normotensive group mean score in Verbal Fluency subtest of MoCA was significantly better than hyperten-

Variable	Mean hypertensive	Mean normotensive	t	df	p	Valid N hypertensive	Valid N normotensive	Std. Dev. hypertensive	Std. Dev. normotensive	F-ratio Variances	p Variances
MoCA score	23.8462	24.1754	-0.57082	120	0.56919	65	57	3.2655	3.07712	1.126183	0.652128
MMSE score	27.6308	27.4561	0.43208	120	0.666461	65	57	2.27465	2.17182	1.09694	0.726438
MoCA - delayed recall	2.2615	2.2456	0.05398	120	0.957038	65	57	1.56402	1.69327	1.172113	0.536801
MoCA - verbal fluency	12.082**	13.9474**	-2.43777	116	0.016296	61	57	3.66194	4.62301	1.593769	0.077395
TMT B	124.7692	120.3333	0.40401	101	0.687061	52	51	52.46572	58.84171	1.257822	0.41718

Figure 4. sCorrelation of blood pressure with cognitive function tests results in older people

sive group (14.04 *vs.* 11.72, t = 3.07, p = 0.002). Rest of differences were not statistically significant (p > 0.05). Statistically significant result is marked with double asterisk (Figure 4).

Blood pressure according to MCI diagnosis

According to what has been said in the Introduction section, diminished level of BP could be a secondary cause of dementia development, probably Alzheimer Disease in particular [17]. Therefore, to exclude patients which may have first signs of dementia in functional dimension, results of screening tests were used. MCI were diagnosed in 47 patients, BP measurements were available in 42. Number of cognitively intact participants were 81, in 77 of them BP measurements were available (Table II).

Table II. Correlation of blood pressure with cognitive function tests results in older people
Diagnosis of patients with BP measurement available (n = 119) according to cognitive functioning

	MCI-diagnosed (n=47)	Cognitively intact (n=81)
DBP	83.09	84.14
SBP	139.88	141.52
PP	56.79	57.37
MAP	101.83	103.08

All BP measurements are slightly higher in cognitively intact group, however, this group outnumbers MCI group (77 to 42 participants in a MCI group). Mean results of BP in group of MCI is slightly lower than in cognitively intact people.

Discussion

Results obtained in Verbal Fluency test are in line with the assumptions of studies mentioned in the Introduction section [10]. Observed results could be attributed to the fact, that worse performance in verbal fluency is one of the initial signs of dementia [9]. Besides, hypertension could be regarded as a factor, which contributes to dementia development in older people [17].

Moreover, according to what has been shown elsewhere [17], mean results of BP in group of MCI is slightly lower, than in cognitively intact people. Probably, this mechanism could be caused by a secondary effect of dementia development, however, we are not able to prove such assumptions based on available data.

Interestingly, longitudinal studies showed significant association between hypertension and composite cognitive score calculated for each subject as the mean sum of the test scores in group of 999 men at 20-year follow-up [8]. The strongest correlation was shown in group of untreated men. However, composite score of cognitive functions was not used in our studies. Contrary, we have evaluated scores from two single subtests of MoCA, to check what specific cognitive functioning domains could be most vulnerable to hypertension. In fact, participants with higher blood pressure did not show worse performance in all cognitive domains, but, instead, perform worse in Verbal Fluency test only. Interestingly, MCI is an umbrella term. Following years of researches resulted in creation of classification of patients into specific types, e.g.: amnestic MCI, multiple-domain MCI, single non-memory MCI and other. Such specification seems to be reasonable because of valuable prognostic value of estimating the risk of progress to dementia of patients with specific MCI type [19]. Therefore, lower BP in a group of MCI-diagnosed patients is a phenomenon, which is worth to consider in further studies with making a distinction between specific MCI types. Moreover, it would be worth to examine this phenomenon in longitudinal manner on larger samples with current treatment and medical history incorporated into analysis.

Conclusions

1. Significant and negative correlation between Diastolic Blood Pressure, Systolic Blood Pressure and results of Verbal Fluency subtest of MoCA test was observed.
2. Mean score of normotensive group was significantly better that mean score of hypertensive group in Verbal Fluency subtest (13.94 vs. 12.08 words).
3. Participants with elevated systolic blood pressure have tend to perform worse on Verbal Fluency Test
4. Mean results of BP in group of MCI is slightly lower than in cognitively intact people.
5. We did not notice any statistically significant correlation between BP and TMT B.

Konflikt interesów / Conflict of interest
Brak/None

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