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***Retrospective Study***

**Analysis of the relationship between blood pressure variability and subtle cognitive decline in older adults**

Guo HF *et al*. Blood pressure variability and cognition

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**Author contributions:** HF Guo and Y Wu analyzed the data and wrote the paper; Li J was responsible for execution and data collection; Pan FF was responsible for the study conception and design; the final version of the manuscript has been approved by all authors. Guo HF and Wu Y contributed equally to this work as co-corresponding authors. The reasons for designating them as co-corresponding authors are as follows: Firstly, this manuscript is a collaborative work. The designation of co-corresponding authorship accurately reflects the distribution of responsibilities and burdens associated with the time and effort required to complete the study and the resultant paper. Secondly, Guo HF and Wu Y contributed equally to this work. The choice of these researchers as co-corresponding authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. Guo HF is responsible for the overall planning and the organization of clinical data, Wu Y is responsible for the data summary and statistical analysis. In summary, we believe that designating Guo HF and Wu Y as co-corresponding authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

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**Abstract**

BACKGROUND

Blood pressure variability (BPV) has been shown to be related to mild cognitive impairment (MCI) and Alzheimer's disease (AD) in a number of studies. However, the relationship between BPV and subtle cognitive decline (SCD) has received minimal attention in this field of research to date and has rarely been reported.

AIM

To examine whether SCD is independently associated with changes in BPV in older adults.

METHODS

Participants were selected based on having participated in cognitive function evaluation and ambulatory blood pressure measurement at the Shanghai Sixth People's Hospital Affiliated with Shanghai Jiao Tong University School of Medicine between June 2020 and August 2022. The participants included 182 individuals with SCD as the experimental group and 237 with normal cognitive function as the control group. The basic data, laboratory examinations, scale tests, and ambulatory blood pressure test results of the two groups were analyzed retrospectively, and the relationship between SCD and BPV was subsequently evaluated.

RESULTS

Significant differences were observed between the two groups of participants (*P* < 0.05) in terms of age, education level, prevalence rate of diabetes, fasting blood glucose level, 24-h systolic blood pressure standard deviation and coefficient of variation, 24-h diastolic blood pressure standard deviation and coefficient of variation. The scale monitoring results showed significant differences in the scores for memory, attention, and visual space between the experimental and control groups. Logistic regression analysis indicated that age, education level, blood sugar level, and BPV were factors influencing cognitive decline. Linear regression analysis showed that there was an independent correlation between blood pressure variation and SCD, even after adjusting for related factors. Each of the above differences was still significant.

CONCLUSION

This study suggests that increased BPV is associated with SCD.

**Key Words:** Blood pressure; Variability; Elderly; Subtle cognitive decline relationship

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**Core Tip:** Cognitive dysfunction is a disease that seriously endangers human health, and its current treatment measures are far from perfect. Early identification, which can facilitate the implementation of early treatment, is the primary focus of this research. Our aim was to explore the correlation between blood pressure variability (BPV) and subtle cognitive decline and to understand whether BPV can be used for early detection of cognitive impairment.

**INTRODUCTION**

Alzheimer's disease (AD) is a highly harmful disease. Epidemiological surveys have shown that there are more than 30 million AD patients globally, and it is expected that in 30 years, this number will have expanded to 130 million. Cognitive impairment resulting from AD is serious and irreversible, carries a high disability rate, and is difficult to cure, placing a huge burden on both families and society as a whole[1,2]. Although much work has already been performed in this area, there remains no truly effective therapy for AD. Early identification, screening, detection, and intervention are important for preventing the progression of the disease[3-6]. The National Institute on Aging and the Alzheimer’s Association have classified AD into three distinct stages[7]:The AD preclinical stage [subjective cognitive decline and subtle cognitive decline (SCD), AD-derived mild cognitive impairment (MCI), and the dementia stage]. SCD refers to the initial phase of cognitive decline. Memory loss is the primary symptom of AD during this period, although a routine examination cannot indicate MCI caused by dementia. According to prior research, early identification and prompt intervention can help prevent 30% of the risk factors associated with AD[4,8,9]. Therefore, SCD has become a popular topic in early-stage AD research. Unlike gene testing, cerebrospinal fluid, and positron emission tomography (PET), blood pressure variability (BPV) testing is inexpensive, non-invasive, and easy for patients to accept. Determining the correlation between BPV and cognitive impairment can provide valuable insight for clinicians regarding the process of diagnosis and treatment.

BPV, also known as blood pressure volatility, indicates the degree to which an individual's blood pressure fluctuates during a certain period of time and does not depend on blood pressure levels[10-12]. BPV is an indicator of spontaneous fluctuations in blood pressure, which are closely related to arterial remodeling, left ventricular hypertrophy, stroke, and hypertensive renal damage. In the physiological process that emerges during the progression from hypertension to cardio-cerebrovascular events, BPV plays an adverse role at every stage[13-16]. Blood pressure changes that occur within 24 h (short-term BPV) are more valuable for predicting the risk of cardiovascular death than clinical blood pressure. Previously published articles have found that the predictive effect of clinical blood pressure is limited, and short-term BPV can serve as a more accurate indicator than clinical blood pressure; therefore, the use of ambulatory blood pressure monitoring (ABPM) should be widely promoted over the use of clinical blood pressure[17-19]. Previous studies have shown that that BPV is associated with MCI and AD[20-22], but studies on BPV and SCD to date have proven rare. SCD is an early stage of AD, and those with SCD face a significantly higher risk of developing MCI and AD people with SCD than those with normal cognitive function[23-25]. Our aim was to evaluate the correlation between BPV and SCD and to analyze whether BPV could be used as a screening index for early cognitive decline.

**MATERIALS AND METHODS**

***Participants***

From June 2020 to August 2022, 1095 people who participated in a routine physical examination at the Department of Geriatrics of Shanghai Sixth People’s Hospital completed the neuropsychological scale test and 24-h ABPM. According to the test results, 237 individuals had normal cognitive function and were classified as the control group (NC), and 182 had SCD and were classified as the experimental group (SCD). The basic data, laboratory examinations, scale tests, and ABPM test results of the SCD and NC groups were retrospectively analyzed, and the relationship between BPV and SCD was subsequently assessed.

**Inclusion criteria:** (1) Participants aged 60 or older; (2) those who have a primary school level education or higher; and (3) those who possess a normal level of hearing and eyesight.

**Exclusion criteria:** (1) Patients with MCI and AD; (2) those with a history of cerebrovascular disease, such as brain trauma, cerebral infarction, cerebral hemorrhage, Parkinson's disease, brain tumor, epileptic psychosis, or dysplasia; (3) those with a Hamilton Depression Rating Scale 17-item score of more than 12; (4) those with other diseases affecting cognitive function, such as B12 deficiency, alcoholism, folic acid, drug abuse, syphilis, and AIDS; (5) those with visual impairment, hearing impairment, and limb dysfunction resulting in an inability to complete the neuropsychological scale; and (6) those with serious diseases in major organs, such as the liver, kidneys, heart, and lungs.

***Clinical-demographic data***

Participants’ sex, age, height, weight, educational attainment, and history of chronic diseases were recorded. On the same day, routine blood tests, blood lipids, liver and kidney function, and blood glucose were checked, and a head magnetic resonance imaging examination was conducted.

***Cognitive function***

In a specialized neuropsychological room, the scale was assessed by trained professionals. Scale detection participants did not participate in the judgment of cognitive diagnosis. Each participant was screened using strict scale tests to assess memory, space, attention, language, execution, and social cognition; the scales utilized included a mini-mental state examination (MMSE), the Chinese version of the Montreal Cognitive Assessment (MoCA; MoCA-CV), Hamilton Depression Scale, Auditory Verbal Learning Test (AVLT), Animal Verbal Fluency Test (AFT), Boston Naming Test (BNT), Symbol Digit Modalities Test (SDMT), Rey-Osterrieth Complex Figure Test (CFT), Trail Making Test Part A (TMT-A) and part B (TMT-B), Prospective Memory Test (PrM), Functional Activities Questionnaire (FAQ), and so on.

***ABPM and BPV indices***

**Twenty-four-hour ABPM:** The testing period was from 7:00 on day one to 7:00 the following day, from 7:00 to 21:59 during the day, and was recorded every 30 minutes. At nighttime, the testing period was from 22:00 to 6:59 on the second day, with tests taken every 60 min. To be included in the group, the valid readings had to be greater than 90%. BPV indices included 24-h systolic blood pressure standard deviation (SBP SD) and coefficient of variation (SBP CV) as well as 24-h diastolic blood pressure standard deviation (DBP SD) and coefficient of variation (DBP CV). The coefficient of variation was calculated using the formula CV = 100 × SD/mean.

***Biochemical indicators***

On the day of the scale test, after fasting for 8 h, venous blood samples were taken and immediately tested for blood glucose (fasting and two hours postprandial blood glucose), blood lipids, serum creatinine, serum uric acid, and so on.

***Diagnostic criteria of SCD***

A total of six neuropsychological scores were examined using the method by Jak and Bondi: the AFT and a 30-item BNT were administered to evaluate language; the TMT-A and TMT-B were administered to evaluate attention/executive function; and two scales were applied to evaluate memory function - the Rey AVLT, a 30-min delayed free recall test, and AVLT recognition. The criteria were used to determine whether participants had SCD: (1) cognitive decline on two of the six neuropsychological measures in different cognitive fields, defined as > 1 SD below the age-corrected normative mean; and (2) a FAQ score of 6-8[23].

***Statistical analysis***

The statistical analysis was conducted using SPSS 24.0. We used the mean ± SD to represent the measurement data, and a *t*-test was applied to compare the NC and SCD groups. A *χ*2 test was utilized to compare the counting data between the two groups. A binary logistic regression was used to analyze the related factors of cognitive impairment, and a multiple linear regression was performed to determine cognitive domain scores were correlated with BPV. The level of significance was set at *P≤* 0.05.

**RESULTS**

***Demographic characteristics of the subjects***

Table 1 presents the general characteristics of the participating researchers. Significant differences were observed in age, education level, incidence of diabetes, fasting blood glucose levels, SBP SD, SBP CV, DBP SD, and DBP CV between the NC ang SCD groups. No significant differences in other indices were observed.

***Cognitive scale score***

As shown in Table 2, a significant difference was observed between the two groups on the MMSE and the MoCA. A comparison of the scores for each cognitive domain revealed significant differences in attention, memory, and visual space between the two groups.

***Analysis of influencing factors of cognitive impairment***

Using cognitive decline as a dependent variable and other influencing factors as independent variables, multivariate logistic regression analysis revealed that cognitive decline was significantly correlated with age, education level, diabetes, SBP SD, DBP SD, SBP CV, and DBP CV (Table 3).

***Effect of blood pressure variation on cognitive performance***

Multiple linear regression analysis demonstrated that memory, attention, and visual-spatial dysfunction in the SCD group were significantly correlated with SBP SD and CV, while DBP SD and CV were significantly correlated with memory impairment. Even adjusting for age, sex, drinking, smoking, education level, body mass index, blood glucose, and blood lipid levels, these differences remained significant (Table 4).

**DISCUSSION**

This study aimed to identify a simple method for detecting cognitive decline in its early stages. In this retrospective study, BPV was observed to be independently associated with SCD and increased BPV in individuals aged 60 or above and may be seen as a risk factor for SCD.

Current reports on the correlation between BPV and cognitive impairment are inconsistent. Most researchers believe that cognitive impairment is associated with increased BPV. However, different views have been expressed on this topic, such as that higher BPV has nothing to do with dementia[26-28]; that patients with increased BPV have higher cognitive scores; and that only the increase in systolic blood pressure variation is related to cognitive decline, while the increase in diastolic blood pressure variation is not. In addition, there are significant differences in the cognitive assessment tools, BPV calculation method, duration of blood pressure monitoring, study population, and sample size among different studies[29-31]. Thus, standardized methods should be considered to compare and determine the significance of various studies. The results of the 24-h ABPM were used to calculate BPV, which is a more objective form of measurement than clinic blood pressure; the equipment is simple, primary medical institutions can use it, and research participants can easily accept this method.

At present, effective treatment for dementia remains far from perfect, and many people with cognitive impairment seek treatment in community medical institutions. Identifying changeable risk factors is important for preventing dementia in primary healthcare institutions. ABPM to evaluate blood pressure levels and BPV is a simple method for assessing the risk of dementia and evaluating the effectiveness of treatment.

There are several viewpoints on the mechanism underlying cognitive impairment caused by BPV[32-36]: (1) Hemodynamic instability has harmful effects on neurovascular units and results in endothelial injury and vascular smooth muscle dysfunction, leading to accelerated neuronal damage and neuronal loss; (2) Arterial remodeling is beneficial to β-amyloid deposition and reactive glial hyperplasia; (3) The fluctuation of arterial blood pressure leads to inconsistent perfusion attacks of tissue hypoxia-ischemia, promoting the activation of microglia and the production of brain amyloid proteins, resulting in neuronal injury and cell death; and (4) Oxidative stress and inflammation. There may be direct connections between vascular and metabolic factors and the deposition of β-amyloid proteins in the brain, promoting oxidative stress and inflammation as well as neurodegeneration.

The results of this study show that BPV can be used as a tool to screen for early-stage cognitive decline; therefore, it is possible to delay or prevent further cognitive decline by improving BPV. The sample size of future studies should be increased and long-term follow-up assessments should be conducted to identify the correlation between BPV and cognitive impairment, especially in primary medical institutions as BPV can be considered a valuable tool for screening for cognitive decline.

This study had several limitations, including that it was a small cohort study and that participants were not randomly selected, which could potentially have biased the results. Other indicators that could have an impact on the results were not used in this study to measure BPV. Cerebrospinal fluid and PET tests were not performed, and variations in blood pressure and intracranial lesions could not be identified. Follow-up work should be carried out to extend the results of the study and determine whether effective control of BPV can reduce or reverse the decline in cognitive function. Effective control of BPV was not considered in this study.

**CONCLUSION**

According to this study, an increase in BPV is one of the risk factors for early cognitive decline. BPV was found to be independently associated with SCD. BPV should be controlled effectively in clinical practice, especially in the treatment of hypertensive patients. The goal is not only to reach a standard blood pressure level but also to steadily reduce blood pressure and control BPV to better protect cognitive function and try to prevent or delay the occurrence of AD.

**ARTICLE HIGHLIGHTS**

***Research background***

Cognitive impairment is a highly harmful disease for which there is no perfect treatment. Early detection and treatment are the main focus of related research. Variation in blood pressure has been correlated with cognitive impairment in previous studies; however, few studies have examined subtle cognitive decline.

***Research motivation***

Our purpose was to analyze the influencing factors for subtle cognitive decline (SCD) and find a simple and effective index through which to assess cognitive decline that can be used to guide clinical work.

***Research objectives***

The study aimed to determine whether blood pressure variability (BPV) leads to cognitive impairment. The results showed that an increase in BPV is independently related to SCD and that BPV may be used as a tool for evaluating cognitive impairment and the effectiveness of treatment.

***Research methods***

We used a standard neuropsychological scale to evaluate cognitive function and retrospectively analyzed the correlation between BPV and SCD.

***Research results***

The results show that increased BPV may be a factor leading to cognitive decline. The results of such studies are rare; however, the sample size is not sufficiently large, and no further research has been carried out to determine whether it can be used as an index to analyze the effectiveness of treatment.

***Research conclusions***

This study demonstrates that BPV is a clinical indicator of early cognitive decline. In this study, 24-h ambulatory blood pressure monitoring test was used as an index from which to calculate BPV, one that is simple, effective, and can be readily used in primary healthcare institutions.

***Research perspectives***

Long-term follow-ups should be considered in the future to further the collective comprehension of the correlation between BPV and cognitive decline and the progress of cognitive impairment as well as to estimate the benefits of improving BPV in the treatment of cognitive impairment.

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**Footnotes**

**Institutional review board statement:** The study was reviewed and approved by the Shanghai Sixth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, approval No. 2022-0326.

**Informed consent statement:** All study participants provided written informed consent for personal and medical data collection prior to study enrollment.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

**Data sharing statement:** The dataset is available from the corresponding author at ghfghm@163.com.

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**Table 1 General characteristics of participants**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **NC (*n* = 237)** | **SCD (*n* = 182)** | ***P* value** |
| Age, yr | 70.35 ± 9.57 | 72.19 ± 10.31 | 0.002 |
| Sex (male, %) | 169 (71.31%) | 127 (69.78%) | 0.219 |
| Education, yr | 11.49 ± 4.12 | 10.05 ± 3.79 | 0.037 |
| BMI (kg/m2) | 22.47 ± 4.91 | 23.16 ± 5.03 | 0.291 |
| Smoking, *n* (%) | 51 (21.52) | 39 (21.43) | 0.479 |
| Drinking, *n* (%) | 72 (30.38) | 57 (31.32) | 0.517 |
| Hypertension, *n* (%) | 104 (43.88) | 83 (45.60) | 0.153 |
| Diabetes, *n* (%) | 35 (14.77) | 31 (17.03) | 0.021 |
| CAD, *n* (%) | 29 (12.24) | 27 (14.84) | 0.149 |
| FBG (mmol/L) | 5.41 ± 1.17 | 5.93 ± 1.61 | 0.037 |
| PBG (mmol/L) | 8.75 ± 2.81 | 8.59 ± 2.63 | 0.275 |
| Scr (µmol/L) | 82.45 ± 29.51 | 79.43 ± 28.72 | 0.117 |
| TC (mmol/L) | 4.53 ± 1.37 | 4.19 ± 0.95 | 0.093 |
| TG (mmol/L) | 1.32 ± 0.75 | 1.42 ± 0.81 | 0.055 |
| HDL-C (mmol/L) | 1.15 ± 0.51 | 1.17 ± 0.49 | 0.213 |
| LDL-C (mmol/L) | 2.39 ± 0.83 | 2.21 ± 0.79 | 0.314 |
| SBP SD | 10.52 ± 2.94 | 14.15 ± 4.37 | 0.000 |
| DBP SD | 7.32 ± 2.74 | 9.45 ± 3.07 | 0.040  |
| SBP CV | 12.35 ± 3.74 | 16.97 ± 4.91 | 0.000 |
| DBP CV | 9.85 ± 2.73 | 12.63 ± 3.81 | 0.006 |

NC: The control group; SCD: Subtle cognitive decline; BMI: Body mass index; CAD: Coronary artery disease; FBG: Fasting blood glucose; PBG: Postprandial blood glucose; Scr: Serum creatinine; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SBP SD: 24-h systolic blood pressure standard deviation; SBP CV: 24-h systolic blood pressure coefficient of variation; DBP SD: 24-h diastolic blood pressure standard deviation; DBP CV: 24-h diastolic blood pressure variation coefficient.

**Table 2 Scores of personnel cognition scale in two groups**

|  |  |  |  |
| --- | --- | --- | --- |
| **Index** | **NC (*n* = 207)** | **SCD (*n* = 175)** | ***F* (*P* value)** |
| MMSE | 28.97 ± 2.13 | 26.15 ± 1.62 | 49.327 (< 0.001) |
| MoCA | 25.74 ± 2.96 | 22.93 ± 3.27 | 57.319 (< 0.001) |
| AVLT recognition | 21.39 ± 5.27 | 19.31 ± 3.77 | 3.572 (0.041) |
| AVLT delayed recall | 6.32 ± 2.29 | 4.17 ± 1.59 | 8.351 (0.011) |
| BNT | 24.15 ± 3.14 | 22.59 ± 3.57 | 0.275 (0.179) |
| SDMT | 39.29 ± 12.57 | 34.26 ± 11.09 | 4.529 (0.032) |
| TMT-A | 53.14 ± 23.95 | 57. 83 ± 26.71 | 0.127 (0.359) |
| TMT-B | 133.49 ± 39.72 | 154.97 ± 45.21 | 5.273 (0.019) |
| Rey CFT copy | 34.59 ± 3.71 | 31.49 ± 4.25 | 8.319 (0.014) |
| Rey CFT recall | 16.72 ± 5.93 | 13.27 ± 6.41 | 9.592 (< 0.001) |
| AFT | 16.79 ± 4.52 | 16.32 ± 4.17 | 0.035 (2.531) |
| PrM | 14.31 ± 4.15 | 12.29 ± 4.52 | 3.572 (0.031) |

NC: The control group; SCD: Subtle cognitive decline; MMSE: Mini-mental State Examination; MoCA: Montreal Cognitive Assessment; AVLT: Auditory Verbal Learning Test; BNT: Boston Naming Test; SDMT: Symbol Digit Modalities Test; TMTA, TMT-B: Trail Making Test Part A and B; Rey CFT: Rey-Osterrieth Complex Figure Text; AFT: Animal Fluency Test; PrM: Prospective Memory Test.

**Table 3 Logistic regression analysis influencing factors of cognitive impairment**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Index** | **β** | **SE** | **Wald** | ***P* value** | **OR** | **95%CI** |
| Age | 0.37 | 0.09 | 17.59 | 0.000 | 1.63 | 1.45-1.81 |
| Education | 0.75 | 0.13 | 20.31 | 0.000 | 1.92 | 1.75-2.31 |
| Diabetes | 0.11 | 0.03 | 13.27 | 0.000 | 1.21 | 1.09-1.37 |
| SBP SD | 1.31 | 0.24 | 26.15 | 0.0000 | 3.95 | 2.57-4.72 |
| SBP CV | 0.95 | 0.21 | 30.63 | 0.000 | 3.71 | 2.69-4.63 |
| DBP SD | 2.47 | 0.61 | 8.59 | 0.023 | 9.72 | 3.51-18.95 |
| DBP CV | 0.85 | 0.19 | 27.33 | 0.002 | 3.01 | 2.65-3.91 |

SBP SD: 24-h systolic blood pressure standard deviation; SBP CV: 24-h systolic blood pressure coefficient of variation; DBP SD: 24-h diastolic blood pressure standard deviation; DBP CV: 24-h diastolic blood pressure coefficient of variation.

**Table 4 Correlation between blood pressure variability and cognitive function by multivariate linear regression analysis**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** |  | **Unadjusted model** | ***P* value** | **Adjusted model 1** | ***P* value** | **Adjusted model 2** | ***P* value** |
| **β (95%CI)** | **β (95%CI)** | **β (95%CI)** |
| Memory | SBP SD  | -0.82 (-1.17 to -0.49) | < 0.001 | -0.57 (-0.91 to -0.22) | < 0.001 | -0.51 (-0.89 to -0.21) | < 0.001 |
| SBP CV | -0.79 (-1.15 to -0.42) | < 0.001 | -0.61 (-0.93 to -0.32) | < 0.001 | -0.59 (-0.91 to -0.25) | < 0.001 |
| DPB SD | -0.31 (-0.56 to -0.07) | < 0.05 | -0.29 (-0.51 to -0.08) | 0.029 | -0.27 (-0.49 to -0.07) | 0.035 |
| DPB CV | -0.27 (-0.55 to 0.01) | 0.037 | -0.26 (-0.47 to -0.08) | 0.041 | -0.23 (-0.41 to -0.03) | 0.049 |
| Language | SBP SD  | 0.04 (-0.02 to 0.09) | 0.155 | 0.03 (-0.01 to 0.07) | 0.165 | 0.03 (-0.02 to 0.09) | 0.172 |
| SBP CV | 0.04 (-0.01 to 0.11) | 0.153 | 0.03 (-0.01 to 0.09） | 0.167 | 0.03 (-0.02 to -0.10) | 0.157 |
| DPB SD | 0.11 (-0.01 to 0.23) | 0.241 | 0.09 (0.02 to 0.19) | 0.305 | 0.09 (0.01 to 0.18) | 0.291 |
| DPB CV | 0.08 (-0.02 to 0.17) | 0.195 | 0.07 (-0.01 to 0.15) | 0.236 | 0.07 (-0.02 to 0.16) | 0.229 |
| Attention | SBP SD  | -0.76 (-1.07 to -0.39) | < 0.001 | -0.67 (-1.03 to -0.21) | < 0.001 | -0.70 (-1.01 to -0.39) | < 0.001 |
| SBP CV | -0.69 (-0.95 to -0.27) | < 0.001 | -0.61 (-0.93 to -0.25) | < 0.001 | -0.59 (-0.87 to -0.31) | < 0.001 |
| DPB SD | -0.17 (-0.35 to 0.02) | 0.09 | -0.11 (-0.32 to 0.01) | 0.13 | -0.12 (-0.31 to 0.02) | 0.13 |
| DPB CV | -0.15 (-0.29 to -0.01) | 0.08 | -0.09 (-0.03 to 0.02) | 0.15 | -0.08 (-0.02 to 0.03) | 0.17 |
| Visuospatial ability | SBP SD  | -0.27 (-0.39 to -0.14) | < 0.01 | -0.21 (-0.35 to -0.10) | < 0.01 | -0.20 (-0.33 to 0.06) | < 0.01 |
| SBP CV | -0.31 (-0.42 to -0.21) | < 0.01 | -0.27 (-0.39 to -0.14) | < 0.01 | -0.22 (-0.40 to -0.05) | < 0.01 |
| DPB SD | -0.11 (-0.25 to -0.03) | 0.147 | -0.07 (-0.02 to 0.03) | 0.163 | -0.06 (-0.02 to 0.01) | 0.179 |
| DPB CV | -0.15 (-0.29 to 0.01) | 0.133 | -0.08 (-0.19 to 0.02) | 0.182 | -0.08 (-0.18 to 0.03) | 0.195 |
| Executive function | SBP SD  | 0.16 (0.05 to 0.28) | 0.217 | 0.12 (-0.02 to 0.23) | 0.327 | 0.11 (-0.01 to 0.27) | 0.401 |
| SBP CV | 0.15 (0.05 to 0.26) | 0.195 | 0.11 (-0.01 to 0.21) | 0.313 | 0.10 (0.01 to 0.0.21) | 0.374 |
| DPB SD | 0.23 (0.09 to 0.39) | 0.291 | 0.19 (0.03 to 0.34) | 0.307 | 0.17 (0.02 to 0.33) | 0.351 |
| DPB CV | 0.19 (0.03 to 0.37) | 0.277 | 0.15 (0.04 to 0.27) | 0.295 | 0.15 (0.04 to 0.29) | 0.283 |
| Social cognition | SBP SD | -0.06 (-0.10 to 0.02) | 0.571 | -0.04 (-0.12 to 0.07) | 0.653 | -0.03 (-0.11 to 0.06) | 0.692 |
| SBP CV | -0.05 (-0.09 to 0.04) | 0.612 | -0.02 (-0.13 to 0.11) | 0.713 | 0.01 (-0.14 to 0.13) | 0.865 |
| DPB SD | 0.17 (0.08 to 0.27) | 0.187 | 0.14 (-0.03 to 0.31) | 0.295 | 0.13 (-0.02 to 0.29) | 0.312 |
| DPB CV | 0.16 (0.04 to 0.29) | 0.203 | 0.13 (-0.01 to 0.30) | 0.323 | 0.12 (-0.02 to 0.27) | 0.371 |

Unadjusted model: Random intercept for the study center. Adjusted model 1: Corrected for age, education, and diabetes. Adjusted model 2: Corrected for age, education, diabetes, body mass index, hypertension, coronary artery disease, smoking, drinking, blood lipids, and serum creatinine levels. SBP SD: 24-hsystolic blood pressure standard deviation; SBP CV: 24-h systolic blood pressure coefficient of variation; DBP SD: 24-h diastolic blood pressure standard deviation; DBP CV: 24-h diastolic blood pressure coefficient of variation.



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