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Blood Pressure and Cognitive Function in Older adults with Cardiovascular Disease

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Abstract

Background—Past studies link elevated blood pressure (BP) and BP variability to adverse neurocognitive changes in community samples. However, little is known about the relationship between BP indices and cognitive function in older CVD patients.

Methods—A total of 99 older adults with CVD completed a comprehensive neuropsychological test battery. Resting BP measurements were collected every 10 minutes for two hours during a separate cardiac assessment. Five BP indices were generated: average and standard deviation of systolic blood pressure, average and standard deviation of diastolic blood pressure, and a function of systolic variability and average diastolic pressure. We examined the relationship between these BP indices and cognitive function.

Results—Partial correlation adjusting for age and education revealed that the function of systolic variability and average diastolic pressure (systolic BP standard deviation divided by the average diastolic BP) was most closely related to test performance, showing significant associations to both Learning/Memory ($r = 0.25$) and Language functioning ($r = 0.22$). Systolic BP indices were also related to Language functioning (SBP avg, $r = 0.22$; SBP sd, $r = 0.25$), though diastolic BP indices were unrelated to performance in any cognitive domain.

Conclusions—The current findings indicate that BP is modestly related to cognitive function in older CVD patients. Contrary to expectations, greater BP variability was associated with better, not poorer, cognitive test performance. Such findings suggest that the relationship between BP and cognitive function is more complicated than typically hypothesized and requires further examination.

Keywords

Blood Pressure; Cognitive Function; Heart Disease

Nearly one-third of adult Americans have hypertension, including more than 50% of people over 60 years of age (National Heart, 2006; Thom et al., 2006). Hypertension will likely become even more prevalent in coming years through the rise in obesity rates and the growing proportion of older adults in America (Harris et al., 2000; Merck Institute of Aging and Health et al., 2004). As a result, medical conditions that are caused or exacerbated by hypertension may also become more prevalent, including end stage renal disease, atrial fibrillation, and congestive heart failure (Heist & Ruskin, 2006; Johnson & Usherwood, 2005).

The increased prevalence of hypertension may also result in greater numbers of persons with poor neurocognitive outcome. Hypertension is a known risk factor for stroke, vascular dementia, and Alzheimer's disease (Peila et al., 2006; Posner et al., 2002). It is associated with numerous adverse brain changes, including greater atrophy and the development of white matter disease (DeCarli, 2003; Gianaros et al., 2006). In terms of cognitive performance, hypertensive individuals exhibit cognitive deficits long prior to the onset of stroke or dementia, particularly on tests of attention, memory and psychomotor speed (Harrington et al., 2000; Knopman et al., 2001; Morris et al., 2002b; Ostrosky-Solis et al., 2001; Waldstein et al., 1991; Elias et al., 2003). Interestingly, recent work suggests that blood pressure (BP) variability may be more closely associated with structural brain changes and cognitive function than hypertension alone (Gunstad et al., 2005; Kanemaru et al., 2001).

Few studies have directly examined the relationship between BP and neuropsychological test performance in older adults with cardiovascular disease (CVD). It appears likely that older CVD patients would be at highest risk for BP-related cognitive problems, as they often have comorbid hypertension and frequently exhibit impairment on cognitive testing (Thom et al., 2006; Trojano et al., 2003; Moser et al., 1999). However, many possible mechanisms for the cognitive deficits in older adults with CVD have been proposed and the specific contribution of BP to cognitive dysfunction remains unclear. Determining the relationship between BP and cognitive function in this population may clarify underlying mechanisms and focus intervention efforts in the future. Based on past findings in other populations, we expected that higher BP levels and greater BP variability would be associated with poorer cognitive function.

Materials and Methods

The following procedures were approved by the local Institutional Review Board and all participants provided written informed consent.

Participants

Participants were 99 older adults enrolled in a longitudinal examination of the neurocognitive consequences of CVD. Participants were recruited from outpatient cardiology clinics and were eligible for participation if they had one or more of the following: myocardial infarction, cardiac surgery, heart failure, coronary artery disease, or hypertension. Individuals were excluded if they had a history of: 1) dementia as defined by a score lower than 24 on the Mini Mental Status Exam (Folstein et al., 1975); 2) history of a major neurological disorder (e.g., Alzheimer disease, stroke); and 3) history of major psychiatric disorder such as schizophrenia, bipolar illness, or substance abuse. Participants averaged 69.20 ± 7.48 years of age and 14.48 ± 2.91 years of education. See Table 1 for demographic and medical characteristics.

Measures

Neuropsychological Tests—Neuropsychological tests were grouped into one of four cognitive domains and raw scores for each test were transformed into z scores based on the mean and standard deviation of our sample. A composite z score for each domain was generated

by averaging z scores from each test. See Table 2 for neuropsychological test performance. Specific cognitive domains included:

- 1) *Language*—Boston Naming Test (Kaplan et al., 1983); Animal Naming (Morris et al., 1989)
- 2) *Visual-Spatial*—Block Design subtest of the Wechsler Adult Intelligence Scale, third edition (WAIS-III; Wechsler, 1997); Hooper Visual Organization Test (Hooper, 1958); Rey Complex Figure Test—Copy (Osterrieth, 1944).
- 3) *Memory*—California Verbal Learning Test learning, short free recall, long free recall, and discrimination (Delis et al., 1987); Brief Visual Memory Test-Revised learning, delayed recall, and discrimination (Benedict, 1997)
- 4) *Attention-Executive-Psychomotor*—Trail Making Test A and B (Army Individual Test Battery, 1944); Stroop Color Word Test, color word trial (Golden, 1978); Controlled Oral Word Association Test (Eslinger et al., 1984); Similarities, Digit Symbol Coding, and Digit Span subtests of WAIS-III (Wechsler, 1997); Grooved Pegboard, dominant hand (Kløve, 1963).

Blood pressure—Participants fasted and held vasoactive medications (e.g. calcium channel blockers, ACE inhibitors), caffeine, and smoking for 6 hours before the cardiac assessment. A standard inflatable BP occlusion cuff was placed around the upper portion of the participant's left arm. Systolic BP and diastolic BP were measured with an automatic, non-invasive monitor, the Pressmate 8800 (Colin Medical Instruments Corp., San Antonio, TX). BP measurements were collected from participants while resting in a fasted state in a quiet, darkened room at 10 minute intervals for two hours. Five blood pressure indices were generated: average and standard deviation of systolic blood pressure, average and standard deviation of diastolic blood pressure, and a function of systolic variability and average diastolic pressure (i.e., systolic BP standard deviation divided by the average diastolic BP) used in past studies (Gunstad et al., 2005).

Procedure

All methods were approved by the local Institutional Review Board and all participants gave written informed consent. Participants provided medical history information through self-report, which was corroborated by medical records wherever possible. Participants then underwent neuropsychological testing by a trained researcher using standardized instructions. BP monitoring was completed during an echocardiogram session on a separate day.

Analytic Plan

A series of analyses were conducted to examine the relationship between BP and cognitive function in older adults with CVD. First, we performed a hierarchical cluster analyses to determine the possibility of subgroups in blood pressure changes during the session (e.g., BP that is stable, BP that decreases over time). Determining whether subgroups of CVD patients show different patterns of BP changes during monitoring would help identify mechanisms for the relationship between BP and cognitive function. Then, partial correlations were computed between all BP indices and each cognitive domain after adjusting for age and education. Finally, to clarify significant relationships, we calculated partial correlations between the derived BP function and specific test scores.

Results

Cluster Analysis of Resting BP Changes

Hierarchical cluster analysis using Euclidean and nearest neighbor distance was utilized to determine the possible presence of subgroups within our sample. As no previous study has examined possible clusters of blood pressure changes in a similar population, we generated solutions for 2 through 6 clusters. See Table 3. These analyses offered no evidence for distinct subgroups within our sample. Therefore, the relationship between BP and cognitive function was examined for the entire sample in subsequent analyses.

BP Indices and Function Across Cognitive Domains

Partial correlations adjusting for age and education showed BP indices were associated with cognitive function. See Table 4. The derived BP variability index was positively related to both Learning/Memory ($r = 0.25$, $p = .01$) and Language functioning ($r = 0.22$, $p = .03$). Both average systolic BP ($r = 0.22$, $p = .03$) and standard deviation of systolic BP ($r = 0.25$, $p = .01$) were also related to Language functioning. No significant relationships emerged between any diastolic blood pressure index and cognitive functioning.

Relationship of BP Variability Index to Specific Cognitive Test Performance

To further clarify the relationship between the derived BP variability index and cognitive function, partial correlations adjusting for age and education were computed for the specific Learning/Memory and Language tests. In terms of Learning/Memory tests, significant relationships emerged between BP variability and multiple CVLT indices [CVLT Learning, $r = 0.21$, $p = .04$; CVLT Long Free Recall, $r = 0.21$, $p = .04$] and BVMT-R indices [BVMT-R Learning, $r = 0.21$, $p = .05$; BVMT-R Delayed Recall, $r = 0.25$, $p = .01$]. See Table 5. In terms of Language performance, analysis showed a non-significant trend between BP variability index and Boston Naming Test [$r = 0.19$, $p = .06$]. No other significant relationships emerged.

Discussion

Results from the present study indicate a modest association between BP indices and cognitive function in older adults with CVD. The relationship is strongest between an index of BP variability that incorporates both systolic and diastolic BP and cognitive tests that assess memory and language abilities. Several aspects of these findings warrant discussion.

First, higher resting systolic BP and greater BP variability were associated with better, not poorer, cognitive performance in our sample of older adults with CVD. Such findings run counter to predictions and the effects of hypertension typically reported in other samples (Morris et al., 2002a; Knopman et al., 2001; Kanemaru et al., 2001; Cicconetti et al., 2004). A likely explanation for this relationship involves the autonomic nervous system (ANS) disruption commonly found in CVD patients. Recent literature links cognitive function to ANS indices such as heart rate and heart rate variability, as persons with greater cardiac vagal control exhibit better attention, working memory, and executive function test performance (Hansen et al., 2004b; Hansen et al., 2003). Similar findings also exist in the psychophysiological literature, including consistent relationships between cognitive function and indices of pupil dilation, heart rate, and skin conductance (Fukuda et al., 2005; Hansen et al., 2004a; Hillman et al., 2003). For example, such studies demonstrate an association between greater heart rate reactivity and improved memory performance (Jennings & Hall, Jr., 1980; Cohen & Waters, 1985), findings similar to those found in the current sample. Based on these findings, it appears likely that the ANS disruption associated with many forms of CVD may contribute to the reduced cognitive function in this population and may also help explain the cognitive benefits

of exercise in sedentary older adults (Colcombe & Kramer, 2003). Additional work is needed to clarify the relatively contribution of ANS function to cognition in older adults with CVD.

Less straightforward are past studies showing a relationship between greater BP variability and the presence of white matter disease on neuroimaging (Gunstad et al., 2005; Goldstein et al., 2005). White matter disease is known to adversely impact cognitive function, particularly abilities such as psychomotor speed and executive function (van den Heuvel et al., 2006; Schmidt et al., 2005). However, a recent study suggests a possible explanation for this complex relationship among BP, white matter changes, and cognitive function. Although BP indices were related to white matter changes in some brain regions in persons with essential hypertension, they were not related to all white matter changes (van Boxtel et al., 2006b). Furthermore, little relationship emerged between white matter changes and cognitive function in that sample after adjusting for demographic variables (van Boxtel et al., 2006a). The authors raise the possibility that different aspects of blood pressure (e.g. mean arterial pressure, pulsatile pressure) can result in white matter changes in different brain regions and thus have differential impact on cognitive function (van Boxtel et al., 2006c). Additional evidence for the differential impact of BP and BP variability on the localization of white matter disease is also found in the literature (Gunstad et al., 2005). Another possible explanation is that greater BP variability in isolation does not result in white matter disease, but does so only in the presence of significant vascular pathology (e.g. endothelial dysfunction, arteriosclerosis). Studies are also needed to determine the relationship between BP indices and neurocognitive changes in patients with specific cardiac condition, as this relationship may differ across patient with congestive heart failure, myocardial infarction, or atrial fibrillation.

A second area of discussion is that the current findings suggest that current BP levels and BP variability are not primary causes of cognitive difficulties in older adults with well-managed CVD. Many other mechanisms for cognitive dysfunction in this population have been proposed, including hypoperfusion and inflammatory processes. Recent work shows that reduced cardiac output is associated with reduced executive function in older CVD patients, suggesting that reductions in systemic blood flow may be linked to cerebral hypoperfusion (Jefferson et al., 2006). Similarly, increased levels of inflammatory markers such as C-reactive protein have also been linked to cognitive dysfunction in older CVD patients (Gunstad et al., 2006). Further work is needed to clarify the relative contribution of these and other mechanisms to the cognitive dysfunction found in older CVD patients.

Findings from the present study are limited in several ways. Our measure of BP variability was relatively unsophisticated and future studies employing ambulatory beat-to-beat measures of BP and cognitive function are needed to better understand this relationship. Also, the participants in the current study were closely followed by their cardiologists and had well-managed BP, and it is possible that with poorly-controlled BP may exhibit different patterns of performance. Finally, longitudinal examination of the relationship between BP and cognitive function in older CVD patients is needed. Studies mapping BP changes to cognitive changes over time may provide greater insight into possible mechanisms of change.

In summary, results from the present study provide preliminary evidence for a relationship between BP variability and cognitive function in older adults with CVD. However, the direction of this relationship runs counter to traditional models and requires further examination.

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Table 1

Demographic and Medical Characteristics of 99 Older Adults with CVD

<i>Demographic</i>	
Age	69.20 ± 7.48
Female, %	39.4
Education	14.48 ± 7.48
<i>Medical</i>	
Cardiac output	4.44 ± 1.03
Atrial fibrillation	12.1
Type 2 diabetes	18.2
Myocardial infarction	50.5
Heart Failure	16.2
Cardiac Surgery	28.3
Hypertension	74.7

Table 2

Neuropsychological Test Performance of 99 Older Adults with CVD

<i>Mini Mental Status Examination</i>	28.68 ± 1.50
<i>Attention/Executive/Psychomotor</i>	
Trail Making Test A	36.91 ± 11.25
Trail Making Test B	93.10 ± 36.43
Stroop Color Word Test—Color Word Trial	32.08 ± 9.70
Controlled Oral Word Association Test	40.55 ± 13.99
Similarities	22.01 ± 5.45
Digit Symbol Coding	56.01 ± 13.00
Digit Span	17.73 ± 3.56
Grooved Pegboard-dominant hand	94.46 ± 26.03
<i>Learning/Memory</i>	
CVLT Learning	45.67 ± 11.24
CVLT Short Free Recall	8.76 ± 3.00
CVLT Long Free Recall	9.08 ± 3.43
CVLT Discrimination	92.10 ± 6.05
BVMT-R Learning	17.63 ± 6.81
BVMT-R Delayed Recall	7.48 ± 2.94
BVMT-R Discrimination	5.14 ± 1.06
<i>Language</i>	
Boston Naming Test	54.66 ± 4.91
Animal Naming	19.72 ± 5.20
<i>Visuospatial</i>	
Block Design	33.39 ± 10.47
Hooper Visual Organization Test	23.91 ± 3.45
Complex Figure Test-Copy	30.55 ± 5.47

Table 3

Number of Older Adults with CVD assigned to Blood Pressure Clusters using Hierarchical Cluster Analysis

Solution	C1	C2	C3	C4	C5	C6
2 Cluster	98	1				
3 Cluster	97	1	1			
4 Cluster	96	1	1	1		
5 Cluster	95	1	1	1	1	
6 Cluster	94	1	1	1	1	1

Table 4
 Partial correlation between BP indices and Standardized Cognitive Test Performance in Older CVD Patients

Cognitive Domain	BP Variability Function	SBP (avg.)	SBP (SD)	DBP (avg.)	DBP (SD)
Attention/Executive/Psychomotor	-.01	.02	-.01	.04	-.02
Learning/Memory	.25*	-.06	.19	-.14	.05
Language	.22*	.22*	.25*	.16	.14
Visuospatial	.19	.01	.18	.02	.18

Note.

* denotes two-tailed significance value $p < .05$.

Table 5

Partial Correlation between Derived BP Variability Index and Standardized Performance on Learning/Memory and Language Tests

Test	BP Variability Index
<i>Learning/Memory</i>	
CVLT Learning	.21*
CVLT Short Free Recall	.15
CVLT Long Free Recall	.21*
CVLT Discrimination	.12
BVMT Learning	.20*
BVMT Delayed Recall	.25*
BVMT Discrimination	.07
<i>Language</i>	
Boston Naming Test	.19
Animal Naming	.17

Note.

* denotes two-tailed significance value $p < .05$.