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Effects of Adult Age and Blood Pressure on Executive Function and Speed of Processing

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Abstract

Previous research has established that the effects of chronically increased blood pressure (BP) on cognition interact with adult age, but the relevant cognitive processes are not well defined. In this cross sectional study, using a sample matched for age, years of education, and sex, 134 individuals with either normal BP ($n = 71$) or chronically high BP ($n = 63$) were categorized into younger (19-39 years), middle-aged (41-58 years), and older (60-79 years) groups. Using a between-subjects ANOVA, covarying for race and years of education, composite measures of executive function and perceptual speed both exhibited age-related decline. The executive function measure, however, was associated with a differential decline in high BP older adults. This result held even when the executive function scores were covaried for speed, demonstrating an independent, age-related effect of higher BP on executive function.

Numerous studies have established that chronically increased blood pressure (BP) and hypertension are associated with decreased performance on behavioral tests of cognitive functioning (M. F. Elias, Elias, Robbins, Wolf, & D'Agostino, 2001; M. F. Elias et al., 2004; Raz, Rodrigue, & Acker, 2003; Raz, Rodrigue, Kennedy, & Acker, 2007; Waldstein & Katzel, 2001; Waldstein, Manuck, Ryan, & Muldoon, 1991). Many aspects of cognition are negatively affected by increased BP, with the decline in performance most clearly evident in measures of fluid (speed-based) cognitive abilities involving attention, learning and memory, and executive function (i.e., planning and maintaining relevant components of information processing while inhibiting irrelevant ones). Crystallized (knowledge-based) and verbal abilities are less vulnerable to BP-related decline (e.g., Elias, P. K., Elias, M. F., Robbins, & Budge, 2004). Increased age is also associated with declines in cognitive performance, especially on speed-based tasks and on tests of executive function (Kramer & Madden, 2008; Madden, 2001; Salthouse, 1996; Salthouse & Madden, 2007). Hypertension-related changes in cognition, however, interact with age-related cognitive changes in ways that are not well understood.

Because the changes in the brain and central nervous system associated with increased BP are progressive, cumulative, and generally irreversible, the negative effects of increasing BP on cognitive performance would be expected to increase as a function of adult age (M. F. Elias et al., 2004). However, the relative contributions of age-related and BP-related effects, in cognitive performance, have been difficult to define. In a large longitudinal study, Alves de Moraes, Szklo, Knopman, and Sato (2002) found that older adults with uncontrolled hypertension exhibited a greater degree of decline, across a 6-year period, relative to normotensive individuals, on a test of perceptual speed. Comparisons between hypertensive and normotensive older adults also suggest a negative effect of increased BP on measures of

memory, executive function, and cognitive speed, especially for older adults whose hypertension is not controlled (Brady, Spiro, & Gaziano, 2005; Saxby, Harrington, McKeith, Wesnes, & Ford, 2003). Brady et al. (2005) proposed that memory retrieval processes are dependent on brain regions in the frontal lobe that may be differentially vulnerable to the combined effects of age and hypertension (Raz et al., 2003, 2007). Younger adults were not included in the Brady et al. study, however, and thus the magnitude of the BP-related effects within this older adult sample may not be greater than those exhibited by younger adults.

In cross-sectional studies in which a younger adult group was included, the data suggest that the negative relation between increasing BP and cognitive performance is *less* pronounced for older adults (M. F. Elias, Robbins, Schultz, & Pierce, 1990; Madden, Langley, Thurston, Whiting, & Blumenthal, 2003; Waldstein et al., 1996). P. K. Elias, D'Agostino, Elias, & Wolf, 1995) proposed that survival and attrition effects may contribute to these observations of the negative effects of increased BP, on cognitive performance, being more pronounced in the younger adult age groups. That is, older adult research participants would be those who were relatively healthy, though hypertensive, having avoided significant cardiovascular disease and related comorbidities that are common with increased age. In addition, some epidemiological studies suggest that *decreased* BP is a risk factor for cognitive decline and cerebrovascular disease (Birns, Markus, & Kalra, 2005; del Ser et al., 2005).

The current study had two main goals. The first was to develop a more precise definition of the differences in cognitive performance associated with relatively higher BP. We were interested in whether the BP-related effects would be associated more closely with elementary perceptual speed, or instead with more complex abilities such as executive function. Although both of these abilities exhibit significant age-related decline, after controlling statistically for perceptual speed, age differences in many tests of cognition, including executive function, are significantly reduced. This pattern suggests that age-related cognitive changes may be due primarily to a generalized, age-related slowing of elementary perceptual processing (Salthouse, 1996; Salthouse, Atkinson, & Berish, 2003). From this perspective, the interaction between BP and age would be reflected primarily in perceptual speed, as observed by Alves de Moraes et al. (2002). Alternatively, if BP affects more frontal-lobe dependent aspects of cognition (Brady, Spiro, & Gaziano, 2005; Raz, Rodrigue, & Acker, 2003; Raz, Rodrigue, Kennedy, & Acker, 2007), then the association between higher BP and age-related decline in executive function measures would be particularly pronounced.

The second goal was to provide additional information regarding the direction of the interaction between age-related cognitive changes and BP. In view of the pronounced age-related decline in speed and executive function (Kramer & Madden, 2008; Madden, 2001; Salthouse, 1996; Salthouse & Madden, 2007), we hypothesized that the effects of relatively higher BP would be expressed as a greater magnitude of age-related decline in cognitive performance.

Method

Participants

Participants were recruited through advertisement in local media, throughout Duke University as well as the surrounding community. All participants lived independently and were in relatively good health.

Screening—All procedures were approved by the Institutional Review Board of the Duke University Medical Center. The participants possessed at least a high school education (12 years), provided written, informed consent, and were paid for their participation. There were 134 participants, categorized into three age groups: 47 younger adults between the ages of 19 and 39 years of age, 44 middle-aged adults between the ages of 41 and 58 years of age, and 43

older adults between the ages of 60 and 79 years of age. Sixty-one percent of the 134 participants were Caucasian, 34% were African American, and 5% were Asian; 53% were women. All participants were screened for corrected visual acuity of at least 20/40 and normal color vision. Because age and BP-related effects may vary across treatment categories (i.e., controlled vs. uncontrolled BP; Brady et al., 2005; Jonas, Blumenthal, Madden, & Serra, 2001), we limited the present study to individuals who were not currently taking medication to control BP. None of the participants were taking any type of medication to control BP for at least four weeks prior to beginning the study. None of the participants began any new medications to control their BP during the course of our study. Participant characteristics are presented in Table 1.

Blood pressure measurement—Blood pressure was measured during each of three separate testing sessions, conducted approximately one week apart, by a trained technician. The first session included medical history screening; the remaining two sessions included the psychometric and cognitive testing. After allowing the participant to relax for 5 min, BP was measured three times, at 2.5 min intervals, during each of the three sessions, using an Accutorr Plus Blood Pressure Monitor (Datascope Corp., Montvale, NJ). During the measurements, participants sat at a table with legs uncrossed and feet on the floor with their arm resting on the table. The cuff was placed on the participant's nondominant arm. An auscultatory measurement was taken concurrently using a stethoscope. The fifth Korotkoff phase was used to indicate DBP. We averaged the three BP measurements within each of the three visits, for both SBP and DBP, and then obtained the final BP measures by averaging the three session-specific values.

To eliminate from our sample those participants who may have medical conditions causing their high BP, participants with relatively high BP (average BP either greater than 130 mm Hg systolic or greater than 85 mm Hg diastolic), received a physical examination through the General Clinical Research Center at Duke University Medical Center. These BP values corresponded to high-normal and Stage 1 hypertensive categories in The Sixth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (1997), which was current at the beginning of this study. This examination included a complete blood count, serum chemistry (including glucose, electrolytes, and creatinine), calcium and lipids, and a urinalysis. In addition, participants were excluded if they reported any of the following conditions: coronary disease, renal disease, arrhythmias, valvular disease, pulmonary disease, diabetes requiring insulin or hypoglycemic agents, cancer (other than skin cancer), drug abuse, alcoholism, or any psychiatric illness. Participants were recruited on a case-control basis, so that, within each age group, individuals with relatively high BP were matched with a normotensive individual. We classified 63 participants as having high blood pressure and 71 as having normal blood pressure. Individuals with an average SBP < 130 mm Hg and DBP < 85 mm Hg in each of the three sessions were considered normotensive. Participants were included in the high blood pressure category if either their average BP, in each of the three sessions, was either > 130 mm Hg for SBP, or > 85 mm Hg for DBP.

Demographic characteristics—To assess the similarity of the three age groups and two BP groups on demographic characteristics, we conducted separate 2 (BP Group: high vs. normal) $\times$ 2 (Age Group: younger vs. middle-aged vs. older adults) between-subjects analysis of variance (ANOVA) on participants' years of age, years of education, raw score on the vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981), mean reaction time (RT) on a computerized digit-symbol coding test (Salthouse, 1992), and the average values for SBP and DBP. The results of these analyses are presented in Table 2. The main effects of BP group were significant for SBP and DBP and were qualified by significant Age Group $\times$ BP Group interactions. These interactions indicated that within each age group, BP was significantly higher for the HBP group relative to the NBP group, p

< 0.001, but the difference between the BP groups was smallest in magnitude for the older adults, due to the rise in BP with age.

The age group main effect was significant for digit symbol RT, years of education, and SBP. Bonferroni-corrected paired comparisons [critical $t(128) = 2.43, p < .05$] indicated that the increase in digit symbol RT across each adjacent age group was significant. For the years of education variable, the increased education for older adults relative to middle-aged adults was significant. For SBP, the comparison between the age groups indicated that middle-aged and older adults had significantly higher SBP than the younger adults.

Cognitive Measures

Our selection of cognitive tasks was based on previous factor analytic studies, which have found that these measures loaded highly on distinct factors representing executive function and elementary perceptual speed (Miyake et al., 2000; Salthouse et al., 2003). The executive measures included: a) verbal fluency (Keil & Kasniak, 2002); b) Trails B minus Trails A, on the Trail-Making task (Heaton, Nelson, Thompson, Burks, & Franklin, 1985; Reitan, 1992); and c) Stroop interference (incongruent RT minus congruent RT; MacLeod, 1991). The speed measures were: a) Trails A, from the Trail-Making task; b) a computerized digit symbol coding task (Salthouse, 1992); and c) the neutral (non-conflict) condition of the Stroop task.

In the verbal fluency task, participants named as many words as possible in 60 sec that either began with a designated letter, or were members of the category provided by the experimenter. Participants completed four trials of this task, in which the letters were *p* and *s*, and the categories were animal names and supermarket items. This test requires cognitive monitoring to prevent the repetition of words already generated (Keil & Kasniak, 2002).

The Stroop task (MacLeod, 1991) was modified for computer administration. On each trial, participants viewed one of four words (*red*, *blue*, *art*, or *game*) presented in the center of the computer screen and indicated, by key-press response, whether the color of the letters was red or blue. There were three conditions: congruent (e.g., the word *red* presented in red), incongruent (e.g., the word *red* presented in blue) and neutral (the word *art* or *game* presented in red or blue). Participants completed 360 test trials (six blocks of 60 trials; 120 trials per condition). Participants responded by pressing one of two keys on the computer keyboard, using the left and right index fingers. The assignment of responses to keys was counterbalanced across participants. The dependent variable was the median RT within each task condition. The task began with a brief set of practice trials, which were not analyzed. This task assesses the inhibition of prepotent responses.

Participants completed two subtests of the Trail-Making task (Reitan, 1992). Trails A consisted of a printed page containing randomly intermixed circles containing the numbers 1 through 25. Without lifting their pencil from the paper, participants began at number 1 and connected the circles in numerical order as quickly as possible without making any errors. If an error was made, the experimenter indicated the error and allowed the participant to correct the mistake and continue the task. Timing did not stop if an error correction was necessary. Trails B was similar except that the page contained the letters A through L and the numbers 1 through 13 randomly intermixed on the page. Participants connected each circle alternating between number and letter (e.g., 1-A-2-B-3-C). This test measures sequencing and planning. The digit symbol coding task (Salthouse, 1992) is a computer-administered, two-choice RT task, similar to the Digit Symbol Substitution subscale of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). A table at the top of the computer screen lists the digits 1 through 9 paired with various symbols (e.g., an 8 paired with an X). This table remains on the screen throughout the entire task, and the digit-symbol pairings are constant. On each trial, a single digit-symbol

pairing appears on the screen, and the participants makes a same/different keypress response regarding whether the pairing corresponds to the table.

Procedure

As mentioned previously, all participants completed three sessions, a screening session and two cognitive testing sessions. During the screening session, participants provided informed consent and health and demographic information. The first BP measurements were taken during this session. During the next two cognitive testing sessions, participants completed the visual acuity screening, and psychometric and executive function tests. The order of administration of the cognitive tasks, across the two cognitive testing sessions, was varied across participants. The duration of each cognitive testing session was approximately 90 min, with appropriate rest breaks. Participants with relatively high BP values returned for an additional visit for the physical examination.

Statistical Analyses

To investigate the interactive effects of chronically increased BP and adult age in cognitive performance, we conducted separate analyses of covariance (ANCOVAs) using race, sex, and years of education as covariates, because these demographic variables have been found to be relevant in previous studies (Waldstein & Katzel, 2001). Age group (younger, middle-aged, and older) and blood pressure group (high BP and normal BP) were between-subjects variables. Because of our relatively small sample size, we used age group and BP group as categorical variables. To define speed and executive functioning, we created composite scores based on three individual tests within each domain.

Results

All analyses were conducted with an alpha level of .05. For the computerized tests, the dependent variable was each participant's median RT of correct responses, in each task condition.

Composite Measures of Executive Function and Perceptual Speed

The composite measure of executive function was comprised of a Stroop interference score (incongruent RT minus congruent RT), attentional set shifting from Trail-Making (Trails B minus Trails A), and verbal fluency (mean number of correct exemplar generations over the four trials). The perceptual speed composite score consisted of RT in ms from the Digit Symbol test, RT in ms from the neutral condition in the Stroop task, and RT in seconds from Trails A.

All of the individual test scores were first converted to *z*-scores based on the mean and standard deviation of the younger adult group (normal BP and high BP participants combined). That is, for each individual participant's raw score on each test, the corresponding younger adults' mean score was subtracted, and the result was divided by the younger adult *SD*. Where necessary, the resulting *z*-scores for individual tests were multiplied by -1, so that negative *z*-scores consistently represented worse performance, relative to younger adults. For both speed and executive function, the resulting three *z*-scores were then averaged to obtain a single composite *z*-score.

Screening for outliers revealed five participants (one middle-aged and four older adults), with *z*-scores that were at least 2.5 standard deviations below the mean of the young adult executive function composite score. No outliers were identified for the speed of processing composite score. These individuals were deleted from all subsequent analyses, resulting in a final sample size of 129 participants; 58 hypertensive and 71 normotensive participants.

Effects of Age and Blood Pressure on Executive Function and Perceptual Speed

Mean values for the composite executive function and speed scores are presented in Figure 1. For executive function, the analysis yielded a significant main effect of age group, $F(2, 120) = 9.55, p < .0001$. Bonferroni-corrected paired comparisons, with $t(120) = 2.43, p < .05$, showed that the executive function z -scores of both the middle-aged adults ($M = -.574$), and the older adults ($M = -.557$), were lower than those of the younger adults. The middle-aged and older adult groups did not differ significantly. The main effect of BP group was not significant. Critically, the Age Group $\times$ BP Group interaction was significant, $F(2, 120) = 4.45, p = .014$. Univariate ANCOVAs conducted within for each age group demonstrated that executive function not vary significantly by BP group for either younger or middle-aged adults. For older adults, however, the main effect of BP was significant, $F(1, 34) = 4.94, p = .03$. In the older adult group, those in the high BP group showed significantly lower executive function ($M = -.95$) compared to the normal BP group ($M = -.25$). Univariate ANCOVAs conducted within each BP group showed that significant variation in lower executive function scores, as a function of age group, were evident only for the high BP group, $F(2, 52) = 19.84, p < .0001$.

Analysis of the perceptual speed composite scores yielded a significant main effect of age group, $F(2, 120) = 4.56, p = .012$. Bonferroni-corrected planned comparisons showed the speed scores of older adults ($M = -.541$) were significantly lower than those of the younger adults; no other comparisons were significant. In the speed score analysis, neither the main effect of BP group nor the Age Group $\times$ BP Group interaction was significant.

Independent Effects of Executive Function

As noted in the Introduction, age-related effects in a variety of cognitive variables, including executive function, are often significantly reduced or even eliminated after controlling for processing speed (Waldstein & Katzel, 2001). To investigate the degree to which our observed differences in executive function, across the age groups and BP groups, were independent of processing speed, we conducted similar ANCOVAs, with the addition of speed of processing composite score as a covariate, along with sex, race, and years of education. In this analysis of executive function, both the main effect of age group, $F(2, 119) = 9.25, p = .0002$, and the Age Group $\times$ BP Group interaction, $F(2, 119) = 4.30, p = .016$, remained significant when the composite speed score was included in the covariates.

Discussion

This research addressed the interaction between chronically higher BP and age-related differences in cognition, with two goals. First, we sought to determine whether the influence of relatively high BP on cognitive performance differed across two components of fluid abilities: speed and executive function. Second, we examined whether the BP-cognition relation occurred in the context of greater age-related cognitive decline (i.e., more pronounced effects for older adults) or instead represented survival and attrition effects (i.e., less pronounced effects for older adults). The results (Figure 1) suggest that the relation between BP and cognition varies across these two fluid abilities, with declines being more pronounced for executive function than for elementary perceptual speed. Further, the decline in executive function associated with higher BP group was evident only for the oldest age group, suggesting an exaggeration of age-related cognitive decline rather than survival and attrition effects.

The significant age-related decline in the speed measure replicates previous demonstration of age-related slowing (Madden, 2001; Salthouse, 1996; Salthouse & Madden, 2007), but the age-related decline did not vary significantly as a function of BP group. For executive function, however, a significant Age Group $\times$ BP group interaction represented a more consistent decline in executive function, with increasing age, for the HBP group than for the NBP group.

Similarly, only within the older adult group was the difference in executive function between the BP groups significant. Although executive function and speed may not be entirely separable (Salthouse et al., 2003), the interaction between age group and BP group illustrated in Figure 1 held even when the composite speed score was controlled statistically, demonstrating a specific effect related to executive function. Thus, although both speed and executive function exhibited some decline as a function of increasing age group, for executive function the age-related decline was driven primarily by the HBP individuals.

We concur with the Brady et al. (2005) proposal that cognitive processes that rely heavily on the structural and functional integrity of the frontal lobe are particularly vulnerable to chronically increased blood pressure. Structural brain imaging studies also suggest that chronically increased BP affects the frontal lobe and leads to decline in executive functions, such as selecting and maintaining task-relevant information (Raz et al., 2003, 2007). The mechanism of BP-related changes in the brain is not entirely clear and may include both a decrease in frontal cortical volume and increase in the number of frontal white matter lesions. It has also been noted that compared to normotensive adults, hypertensive adults show a different pattern of cerebral blood flow (Jennings et al., 1998; Waldstein, 1995). However, it should be noted that executive function is not synonymous with frontal lobe function (Rabbitt, 1997), and it is likely that executive function is not strictly limited to the frontal lobe but also relies on cortical networks distributed widely throughout the brain.

The present results support the view that the effects of chronically increased BP interact with those of age by exaggerating the cumulative effects of aging in the brain and central nervous system (Raz et al., 2003, 2007). In some previous studies, in contrast, the negative effects of increased BP are less pronounced for older adults than for younger or middle-aged adults, suggesting that HBP older adult research participants may be those who have survived cardiovascular or other co-morbidities that influence the performance of younger individuals (M. F. Elias et al., 2004). It may also be the case, however, that younger adults may be differentially impaired due to a genetic risk for hypertension resulting in a form of early-onset hypertension that may be more severe than hypertension occurring later in life (Waldstein, 1995). The reasons for the appearance of these different forms of the interaction between adult age and BP, in cognitive performance, are not clear. Some evidence consistent with a survival/attrition effect may be evident in Figure 1 (Panel B), in which the magnitude of age-related decline in the composite speed measure was (nonsignificantly) greater for the NBP group than for the HBP group.

This study has several limitations, including a relatively small sample size and unequal representation of races within each group. In addition, the participants in this study are not representative of the general population, but instead are more highly educated and healthier, and thus likely to possess greater cognitive reserve (Christensen, Anstey, Leach, & Mackinnon, 2008). We attempted to minimize these limitations by focusing on the differences defined by group categorization and including relevant demographic variables as covariates. Even within this relatively healthy group of older adults, however, interactive effects of BP and executive function were evident, and thus the present findings should be a conservative estimate of the BP-related effects in the more general population.

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Figure 1.

Composite scores for executive function (Panel A) and speed (Panel B) as a function of age group and blood pressure group. NBP = normal blood pressure; HBP = high blood pressure. Scores are expressed as standard deviation units (z), relative to the mean of the younger adult group (NBP and HBP combined). Error bars represent 1 SE .

Table 1

Participant Characteristics

Variable	Younger		Group Middle-Aged		Older	
	NBP	HBP	NBP	HBP	NBP	HBP
Age						
Mean	29.50	29.33	46.69	49.24	67.77	68.09
Standard Deviation	5.60	5.75	3.82	4.67	5.06	4.67
Education						
Mean	16.35	16.62	15.17	15.48	16.77	16.62
Standard Deviation	2.42	2.38	2.71	2.46	2.33	3.04
Vocabulary						
Mean	62.16	60.76	61.74	60.19	65.23	62.24
Standard Deviation	6.19	6.53	6.90	6.67	4.12	5.88
Digit-Symbol						
Mean	1424.23	1385.76	1586.17	1593.43	1742.18	1876.05
Standard Deviation	217.16	152.31	229.05	238.22	318.76	335.51
Systolic BP						
Mean	109.01	138.55	113.87	145.17	117.87	139.11
Standard Deviation	9.71	4.76	8.67	11.81	7.94	6.77
Diastolic BP						
Mean	68.48	86.51	72.33	86.58	71.72	79.47
Standard Deviation	7.99	7.19	5.69	8.93	4.46	8.79
Sex						
Total Male	13	11	10	8	9	12
Total Female	13	10	13	13	13	9
Race						
Total Caucasian	11	9	14	9	19	20
Total African-American	9	11	9	12	3	1
Total Asian	6	1	0	0	0	0

Note. NBP = normal blood pressure; HBP = high blood pressure; younger $n = 47$ (26 NBP, 21 HBP); middle-aged $n = 44$ (23 NBP, 21 HBP); older $n = 43$ (22 NBP, 21 HBP); units for Age and Education are years; Vocabulary = raw score on the subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981); Digit Symbol = mean RT on a computerized digit-symbol coding test (Salthouse, 1992); Systolic BP = systolic blood pressure in mm Hg; Diastolic BP = diastolic BP in mm Hg.

Table 2

Results of Between-Subjects ANOVA on Participant Characteristics

Years of Age	df	F	P
BP Group	1	1.08	.300
Age Group	2	667.77**	< .0001
BP Group $\times$ Age Group	2	.94	.395
Error	128	(24.81)	
Years of Education			
BP Group	1	.10	.752
Age Group	2	3.64*	.029
BP Group $\times$ Age Group	2	.11	.898
Error	128	(6.56)	
Mean Vocabulary			
BP Group	1	3.43	.067
Age Group	2	2.55	.082
BP Group $\times$ Age Group	2	.23	.792
Error	128	(37.45)	
Digit Symbol			
BP Group	1	.60	.441
Age Group	2	28.06**	< .0001
BP Group $\times$ Age Group	2	1.35	.262
Error	128	(64978.40)	
Systolic BP			
BP Group	1	336.42**	< .0001
Age Group	2	5.76**	.004
BP Group $\times$ Age Group	2	4.24*	.017
Error	128	(74.15)	
Diastolic BP			
BP Group	1	110.15**	< .0001
Age Group	2	2.99	.054
BP Group $\times$ Age Group	2	5.57**	.005
Error	128	(53.90)	

Note. Values in parentheses are mean square errors.

BP = blood pressure.

*
p < .05.

**
p < .01