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Effects of Age and Hypertension Status on Cognition: The Veterans Affairs Normative Aging Study

Christopher B. Brady

Veterans Affairs Boston Healthcare System and Harvard
Medical School

Avron Spiro, III

Veterans Affairs Boston Healthcare System and
Boston University School of Public Health

J. Michael Gaziano

Veterans Affairs Boston Healthcare System and Harvard Medical School

The authors examined the influence of age and hypertensive status (normotensive, controlled, untreated, or uncontrolled) on several cognitive tests via multiple regression in 357 nondemented, community-dwelling older men (mean age = 67 years) whose hypertensive status was stable over 3 years and who had no medical comorbidities. Age was negatively associated with performance on all but 1 test. Age interacted with hypertensive status on verbal fluency and word list immediate recall; older uncontrolled hypertensives exhibited significantly larger age decrements on these tests compared with normotensives. These findings suggest that uncontrolled hypertension produces specific cognitive deficits beyond those attributable to age alone. These and previous findings illustrate that health conditions such as hypertension should be regularly considered in studies of “normal” cognitive aging.

Keywords: aging, cognition, hypertension

Hypertension is the most prevalent vascular disease risk factor in older adults, affecting 60% of adults aged 60 years and older (National Center for Health Statistics, 1994). The criteria for diagnosing hypertension (per the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [JNC]; Chobanian et al., 2003) are having a systolic blood pressure (SBP) greater than or equal to 140 mmHg, having a

diastolic blood pressure (DBP) greater than or equal to 90 mmHg, and/or taking antihypertensive medication. Recent reports about hypertension prevalence, awareness, treatment, and control (i.e., normalization of blood pressure as a result of treatment) show that, in older adults with hypertension, 31% are unaware, 12% are aware but untreated, 37% are treated but uncontrolled, and only 19% are treated and controlled (Hyman & Pavlik, 2001). Therefore, approximately 80% of older hypertensives have high blood pressure because either they do not know that they are hypertensive or they are not properly treated (see also Egan, Lackland, & Cutler, 2003). Furthermore, with increasing age, hypertension prevalence increases, whereas the proportion of hypertensives with controlled BP decreases (Burt et al., 1995).

Hypertension has negative effects on specific cognitive functions. The effect of hypertension on cognition has been fairly extensively examined in prior studies comparing normotensives (i.e., persons with SBP and DBP less than 140 and 90 mmHg, respectively) with hypertensives. Typically, the hypertensives either are newly diagnosed and still untreated or are removed from their hypertension medications prior to testing. Further, support for a link between blood pressure and cognition comes from numerous studies showing an inverse relation between blood pressure level and cognition (i.e., higher blood pressures are associated with lower cognitive function). The specific cognitive functions affected by high blood pressure have not yet been thoroughly or unequivocally determined; however, high blood pressure is consistently related to deficits in attention (e.g., Madden & Blumenthal, 1998), learning and memory (e.g., P. K. Elias, Elias, D’Agostino, & Cupples, 1997; Swan, Carmelli, & Larue, 1998), some visuospatial functions (e.g., M. F. Elias, Robbins, Elias, & Streeten, 1998), and abstract reasoning and other executive functions (e.g., P. K. Elias et al., 1997; Raz, Rodrigue, & Acker, 2003; Waldstein et al., 1996). Deficits in other cognitive domains (e.g.,

Christopher B. Brady and J. Michael Gaziano, Veterans Affairs Boston Healthcare System and Harvard Medical School; Avron Spiro, III, Veterans Affairs Boston Healthcare System and School of Public Health, Boston University.

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Correspondence concerning this article may be sent to Christopher B. Brady, Geriatric Research, Education, and Clinical Center (182), Veterans Affairs Boston Healthcare System, 150 South Huntington Avenue, Boston, MA 02130. E-mail: christopher_brady@hms.harvard.edu

cognitive processing speed) have been less consistently demonstrated or have not been extensively examined (e.g., language).

The effect of hypertension treatment on cognition has also been examined (e.g., Amenta, Mignini, Rabbia, Tomassoni, & Veglio, 2002; Applegate et al., 1994; Muldoon, Waldstein, & Jennings, 1995; Muldoon et al., 2002; Murray et al., 2002; Schultz, Elias, Robbins, Streeten, & Blakeman, 1989). Although early work suggested that certain classes of hypertension medication negatively affected cognition (e.g., beta-blockers), recent work has been less conclusive, demonstrating that hypertension treatment has little negative effect (e.g., Muldoon et al., 2002), no effect (e.g., Applegate et al., 1994; Muldoon et al., 2002; Schultz et al., 1989) or a protective effect (e.g., Amenta et al., 2002; Muldoon et al., 2002; Murray et al., 2002) on cognition. Therefore, it appears that hypertension medications do not have substantial and consistent negative effects on cognition; however, most of the research to date has been conducted on younger rather than older samples.

Given the high prevalence of hypertension in older adults and the substantial evidence of its impact on cognition, it is somewhat surprising that the hypertension treatment status of older adult samples is not regularly considered in the psychological literature on cognitive aging (a similar argument could be made for other prevalent health conditions in older adults, e.g., diabetes mellitus and cardiovascular disease). Furthermore, relatively little work has examined cognition in naturally occurring subgroups of older adult hypertensives defined by their blood pressure/treatment status (i.e., controlled, untreated, and uncontrolled) relative to a normotensive control group. On the basis of the results of Burt et al. (1995) and Hyman and Pavlik (2001), described above, it seems essential to examine age differences in cognition as a function of hypertension status, such as in hypertensives whose blood pressure is or is not controlled, relative to normotensives. Additionally, it has been argued that the degree of blood pressure control is a potentially critical long-term determinant of cognitive performance in hypertensives (e.g., Waldstein & Katzel, 2001). Thus, examining the effects of hypertension treatment status on cognition would further elucidate the nature of age and blood pressure effects seen in cognitive aging studies of community-dwelling older adults.

In a previous study, we (Brady, Spiro, McGlinchey-Berroth, Milberg, & Gaziano, 2001) found that stroke risk, defined as a composite of vascular disease risk factors (e.g., SBP, diabetes mellitus), predicted 3-year decline in verbal fluency (category) performance beyond that attributable to age in nondemented, stroke-free, community-dwelling older men. The present work is an extension of these findings to examine the effect on cognition of a specific vascular disease risk factor, hypertension, in well-defined groups of normotensive and hypertensive older men without medical comorbidities participating in an ongoing study of aging. We examined the following question: Do age effects on cognition vary as a function of hypertensive status (i.e., normotensive, controlled, untreated, and uncontrolled)?

Method

The Department of Veterans Affairs (VA) Normative Aging Study (NAS) is an ongoing longitudinal study begun in 1963 on a cohort of 2,280 initially healthy men between the ages of 21 and 80 years. The NAS has collected extensive medical, psychological, and lifestyle information during periodic examinations of these men for over 40 years. Details on the recruitment of participants and the study protocol have been described

elsewhere (Bossé, Ekerdt, & Silbert, 1984). It is important to note that all participants were optimally healthy at study entry, meaning that they were free of cardiac disease, hypertension, cataracts, and loss of hearing and had no abnormal laboratory tests (e.g., liver function). Furthermore, although most participants are veterans, only about 5% receive medical care from the VA.

Beginning in 1993, a battery of neuropsychological tests (see Payton, Riggs, Spiro, Weiss, & Hu, 1998; Riggs, Spiro, Tucker, & Rush, 1996, for a description) was administered to continuing participants (approximately 1,000) at each examination to assess the effects of aging and disease on cognition. The battery was analogous to the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery (Morris et al., 1989), with additional measures. We selected men who received the cognitive battery in the initial 1993–1995 examination period to maximize the sample size, given our selection criteria described below.

Sample

We were interested in examining the effects of hypertensive status on cognition in community-dwelling older men who had a stable hypertensive status over two successive exams (1990–1992, 1993–1995) to control for the potential effects on cognition of fluctuating blood pressure and treatment status (e.g., incident hypertension). We used the JNC criteria (JNC-VII; Chobanian et al., 2003) to assign men to normotensive or hypertensive groups. These criteria define hypertension as having an SBP greater than or equal 140 mmHg, having a DBP greater than or equal 90 mmHg, and/or taking antihypertensive medication. Although JNC-VII defines an SBP of between 120 and 139 mmHg as prehypertension, we categorized men with these values as normotensive because JNC-VII does not recommend treatment in men with these SBP values and no other risk factors, such as those in the present study. On the basis of their blood pressure and treatment history, men were assigned to four mutually exclusive blood pressure categories: normotensive (i.e., normal blood pressure, no medication), controlled hypertensive (i.e., normal blood pressure, medication), untreated hypertensive (i.e., high blood pressure, no medication), and uncontrolled hypertensive (i.e., high blood pressure, medication).

We selected stable normotensives and hypertensives without medical comorbidities, such as cardiovascular disease, diabetes mellitus, stroke, or dementia (on the basis of their NAS medical examination and history; see below) to control for the confounding effects of other medical conditions (e.g., diabetes; P. K. Elias et al., 1997) on cognition. Cardiovascular disease was determined via the medical history, the physical examination, and the electrocardiogram. Diabetes mellitus was assessed by the medical history, physical examination, and blood tests. We also excluded persons with a fasting blood glucose of greater than 126 mg/dL to reduce the risk of including undiagnosed diabetics or persons in a prediabetic state (American Diabetes Association, 2003). Stroke was assessed by the medical history and neurological examination. The presence of dementia was determined through the clinical judgment of the internist or the psychiatrist administering the neuropsychological battery or via the report of the participant's family. We used an additional screening criterion of a score of less than 24 on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975), which is a commonly used cut-off score to screen for dementia. Therefore, our sample was 357 (203 normotensives, 34 controlled hypertensives, 75 untreated hypertensives, 45 uncontrolled hypertensives) men aged 52–85 years, with a stable hypertensive status over at least a 3-year interval, who were administered at least one test from the neuropsychological battery during 1993–1995 and who were free of cardiac disease, diabetes, stroke, and dementia across both visits.

Procedure

Measures. During each visit, a board-certified internist conducted a standardized clinical exam that included a medical history, review of

systems, electrocardiogram, physical and neurological exams, and chest X-ray. The details of this medical examination have been described elsewhere (Bossé et al., 1984). Laboratory tests for fasting and 2-hr postchallenge (100 g) glucose levels were conducted on blood samples drawn after an overnight fast. Blood pressure was measured with a standard mercury sphygmomanometer with a 14-cm cuff. A larger cuff was used for men with arms that were too large for the standard cuff. SBP and fifth-phase DBP were measured to the nearest 2 mmHg. SBP and DBP were assessed in both arms sequentially while the participant was sitting and from the right arm while he was standing and in a supine position. The average of measures taken sequentially in each arm while the participant was sitting was used to assign men to the four blood pressure categories.

The neuropsychological battery assessed several cognitive domains, which allowed us to examine whether the effects of hypertensive status on cognition were global or domain specific. *Category fluency (animals)* was used as an index of executive function. In this task, participants were asked to rapidly retrieve exemplars from a semantic category; they were given 60 s to verbally generate a list of unique animal names. The dependent variable was the number of correct items generated. The Digit Span Backward subtest from the Wechsler Adult Intelligence Scale—Revised (WAIS-R; Wechsler, 1981) and a 10-item word list learning test with both immediate and delayed recall trials were used as memory measures. The Digit Span Backward subtest from the WAIS-R required participants to simultaneously maintain and manipulate verbal information in working memory. Persons were given a series of single-digit numbers (e.g., 4, 2) and were asked to repeat the series in reverse order (e.g., 2, 4). The series started at two digits and progressed to a maximum of eight. Two trials were given at each series level, and if a person correctly remembered at least one of the two trials, then the next level was given. If a person missed two trials of the same series, then the test was discontinued. The dependent variable was the highest digit span correctly remembered (e.g., for 2, 4, the score would be 2). In the Word List Learning test from the CERAD battery, 10 words were presented on a computer screen, 1 word per second, for immediate recall. Three recall trials of the same word list were given, and the number of items recalled for each trial was recorded. Recall was tested again after a delay of 5 min. Dependent variables were the number of items recalled from the third trial, for an immediate recall measure, and the number of items recalled after the delay, for a delayed recall measure.

Visuospatial functions were assessed with a speeded pattern comparison test from the Neurobehavioral Evaluation System—Version 2 (Letz, 1991) and a figure-copying test comprising items from the CERAD battery and the Developmental Test of Visual Motor Integration (VMI; Beery, 1989). On the pattern comparison test, participants were visually presented with three patterns (two identical, one different) side by side on a computer monitor and had to make a speeded response as to which was the odd pattern. Their response was recorded by a manual key press. We used the mean response latency (measured in seconds) of correct trials as the dependent variable. For the figure-copying tests, participants were presented with line drawings (e.g., circle, diamond, cube) to copy. Each drawing was scored for accuracy according to the CERAD and VMI scoring criteria, and the score from each drawing was summed to produce a total score that was used as the dependent variable.

Data analyses. We used multiple regression to examine the relation between hypertension status and cognitive measures. In these analyses, the three hypertension groups were compared with normotensives. Age (centered at 65), education (in years), alcohol (current drinker: yes/no; drinks per day), and cigarette use (current smoker: yes/no; former smoker: yes/no) were included as covariates. In preliminary analyses, we also examined the possibility of a quadratic age effect (hence the centering of age to reduce any collinearity between the linear and quadratic age terms). It was significant only for pattern recognition reaction time (RT; mean). In all models, we also included an interaction between hypertension group and age to address the possibility that the effects of hypertension and its treatment varied by age. An alpha level of .05 was used for all statistical tests. Because not all participants completed all of the tests, different numbers of participants were included in each analysis.

Results

Table 1 presents demographic, biomedical, and cognitive indices for the four blood pressure/treatment groups (i.e., normotensive, controlled, untreated, and uncontrolled hypertensives). Across the four groups, there were significant differences only in

Table 1
Demographic, Blood Pressure, and Cognitive Test Scores by Blood Pressure Group (n = 357)

| Variable | Normal blood pressure | | | | High blood pressure | | | | η^2 | <i>p</i> |
|--|---------------------------|-----------|--------------------------------------|-----------|-------------------------------------|-----------|--|-----------|----------|-----------|
| | Normotensive ^a | | Controlled hypertensive ^b | | Untreated hypertensive ^a | | Uncontrolled hypertensive ^b | | | |
| | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> | <i>M</i> | <i>SD</i> | | |
| Age (years) | 66.0 | 7.0 | 68.6 | 6.0 | 68.4 | 7.5 | 69.5 | 6.1 | .04 | .002 |
| Education (years) | 14.4 | 2.6 | 14.7 | 2.4 | 13.8 | 2.6 | 14.5 | 3.1 | .01 | <i>ns</i> |
| SBP (mmHg) | 124.4 | 9.4 | 127.2 | 7.9 | 156.8 | 16.1 | 153.2 | 14.3 | .61 | .0001 |
| DBP (mmHg) | 78.5 | 5.9 | 77.8 | 8.1 | 89.1 | 11.0 | 89.0 | 9.4 | .29 | .0001 |
| HT meds (no.) | | | 1.6 | 0.2 | | | 1.4 | 0.6 | .01 | <i>ns</i> |
| HT treatment (years) | | | 5.2 | 3.1 | | | 5.8 | 4.2 | .01 | <i>ns</i> |
| CF (no. of items generated) ^c | 19.0 | 5.2 | 19.0 | 4.5 | 18.8 | 5.2 | 17.6 | 5.6 | .01 | <i>ns</i> |
| DSB (longest span recalled) ^c | 5.4 | 1.4 | 5.4 | 1.6 | 4.9 | 1.3 | 5.0 | 1.3 | .02 | <i>ns</i> |
| WLIR (no. recalled) ^c | 7.9 | 1.4 | 7.8 | 1.1 | 7.7 | 1.3 | 7.3 | 1.6 | .02 | <i>ns</i> |
| WLDR (no. recalled) ^c | 6.6 | 1.8 | 6.7 | 1.9 | 6.6 | 1.9 | 5.9 | 1.7 | .02 | <i>ns</i> |
| PCRT (s) ^c | 5.5 | 1.5 | 5.8 | 1.8 | 5.8 | 1.7 | 5.5 | 1.1 | .01 | <i>ns</i> |
| FC (total score) ^c | 15.6 | 5.5 | 14.4 | 6.2 | 14.8 | 5.7 | 15.0 | 5.0 | .01 | <i>ns</i> |

Note. Eta = squared values represent the effect size for the blood pressure group factor. SBP = systolic blood pressure; DBP = diastolic blood pressure; HT meds = hypertension medications; no. = number; CF = category fluency; DSB = Digit Span Backward; WLIR = word list immediate recall; WLDR = word list delayed recall; PCRT = pattern comparison reaction time; s = seconds; FC = figure copy.

^a Did not receive treatment. ^b Received treatment. ^c Raw score.

Table 2
Summary of Simultaneous Regression Analyses for Age, Education, and Hypertension Status Predicting Each Cognitive Measure

| Predictor | CF (no. of items generated) | DSB (longest span recalled) | WLIR (no. recalled) | WLDR (no. recalled) | PCRT (s) | FC (total score) |
|-------------------------------------|--------------------------------|--------------------------------|------------------------|------------------------|----------|------------------|
| Intercept | 15.46 | 5.04 | 7.33 | 6.33 | 5.80 | 13.65 |
| Age (years) ^a | | | | | | |
| <i>B</i> | -0.16 | -0.01 | -0.06 | -0.09 | 0.07 | -0.17 |
| <i>SE</i> | 0.05** | 0.02 | 0.02*** | 0.02*** | 0.02*** | 0.06** |
| Education (years) | | | | | | |
| <i>B</i> | 0.26 | 0.02 | 0.04 | 0.02 | -0.04 | 0.14 |
| <i>SE</i> | 0.11* | 0.03 | 0.03 | 0.03 | 0.03 | 0.12 |
| CHT ^b | | | | | | |
| <i>B</i> | -0.36 | -0.01 | -0.07 | 0.27 | 0.20 | -1.96 |
| <i>SE</i> | 1.13 | 0.34 | 0.30 | 0.39 | 0.32 | 1.45 |
| UTHT ^b | | | | | | |
| <i>B</i> | 0.07 | -0.46 | -0.15 | 0.27 | -0.12 | -0.62 |
| <i>SE</i> | 0.81 | 0.24 | 0.22 | 0.28 | 0.23 | 0.85 |
| UCHT ^b | | | | | | |
| <i>B</i> | 0.85 | -0.19 | -0.01 | -0.09 | -0.26 | 0.01 |
| <i>SE</i> | 1.07 | 0.32 | 0.29 | 0.37 | 0.30 | 1.18 |
| Age × CHT interaction ^b | | | | | | |
| <i>B</i> | 0.18 | 0.03 | 0.05 | 0.00 | -0.02 | 0.33 |
| <i>SE</i> | 0.16 | 0.05 | 0.04 | 0.06 | 0.04 | 0.22 |
| Age × UTHT interaction ^b | | | | | | |
| <i>B</i> | 0.10 | 0.02 | 0.04 | 0.02 | -0.01 | 0.13 |
| <i>SE</i> | 0.10 | 0.03 | 0.03 | 0.03 | 0.03 | 0.11 |
| Age × UCHT interaction ^b | | | | | | |
| <i>B</i> | -0.38 | -0.02 | -0.08 | -0.06 | -0.02 | 0.00 |
| <i>SE</i> | 0.14** | 0.04 | 0.04* | 0.05 | 0.04 | 0.16 |
| <i>n</i> | 305 | 267 | 304 | 301 | 300 | 295 |
| <i>R</i> ² | .12 | .03 | .13 | .14 | .21 | .05 |

Note. CF = category fluency; no. = number; DSB = Digit Span Backward; WLIR = word list immediate recall; WLDR = word list delayed recall; PCRT = pattern comparison reaction time; s = seconds; FC = figure copy; CHT = controlled hypertension; UTHT = untreated hypertension; UCHT = uncontrolled hypertension.

^a Centered at 65. The age quadratic trend was significant only for PCRT ($B = 0.004, p < .01$) and was not included in the other models. ^b Relative to normotensives.

* $p < .05$. ** $p < .01$. *** $p < .001$.

age and blood pressure. The cognitive test scores were similar across the four groups in both uncorrected and age-corrected analyses of variance ($ps > .1$).¹

There were no differences in the extent or type of hypertension treatment between the controlled and uncontrolled hypertensive groups. The two groups did not differ in the number of hypertension medications taken, $t(77) = 0.3, p > .1$, or in the duration of treatment, $t(77) = -0.7, p > .1$ (see Table 1). Additionally, there were no differences in the degree of hypertensive therapy (i.e., single vs. multiple medications) between the controlled (65% vs. 35%, respectively) and uncontrolled (71% vs. 29%, respectively) hypertensives, $\chi^2(1, N = 79) = 0.3, p > .1$. The classes of antihypertensives taken by the controlled and uncontrolled hypertensives were also similar (respectively, the proportions were as follows: beta-blocker, 39% vs. 26%; calcium channel blocker, 8% vs. 13%; angiotensin converting enzyme inhibitor, 8% vs. 12%; diuretic, 30% vs. 13%; and alpha adrenergic blocker, 8% vs. 13%; all $ps \geq .1$).

Our initial regression analyses with all covariates showed that alcohol and cigarette use were not significant (all $ps > .1$), and, consequently, we removed them from the models. The subsequent regression models retained age and education as covariates. Table 2 presents the results of the regression analyses of test performance. Across all of the tests except Digit Span, age was nega-

tively associated with performance. A quadratic relation with age was found only for pattern comparison response latency, indicating that response latencies slowed at an accelerating rate with increasing age.

Although there was no main effect for hypertension group, there was a significant Age × Hypertension Group interaction for category fluency and word list immediate recall. In particular, with increasing age, uncontrolled hypertensives exhibited larger age decrements on category fluency and word list immediate recall, compared with normotensives. The regression coefficients for age and for the interaction between age and uncontrolled hypertension in Table 2 show that the age decrements were 2.4 times greater for category fluency (i.e., $-.16$ vs. $-.38$, respectively) and 1.3 times greater for word list immediate recall (i.e., $-.06$ vs. $-.08$, respectively) in the uncontrolled hypertensive group. The analogous Age × Hypertension Group interaction was not significant for

¹ For each analysis, the samples sizes for normotensives and controlled, untreated, and uncontrolled hypertensives were as follows, respectively: category fluency, 178, 27, 61, 39; Digit Span Backward, 157, 24, 53, 33; word list immediate recall, 176, 27, 62, 39; word list delayed recall, 174, 27, 62, 38; pattern comparison RT, 176, 26, 60, 38; and figure copy, 170, 24, 66, 35.

controlled and untreated hypertensives. Furthermore, for pattern comparison, there was no significant interaction between the age quadratic and hypertensive status ($p > .1$).

The Age \times Hypertension Group interactions for category fluency and word list immediate recall are graphically presented in Figure 1. Using the regression models in Table 2, we estimated the predicted values by age for category fluency and word list immediate recall. Because controlled and untreated hypertensives did

not differ from normotensives, we combined these three groups. The predicted values for category fluency and word list immediate recall are plotted in the upper and lower panels of Figure 1, respectively, showing the nature of the Age \times Hypertension group interaction. The age range for each graph is 60–80 years, which is the age range for which all groups had observations. The upper panel of Figure 1 shows the increasing age differences for category fluency for the uncontrolled hypertensives relative to the combined

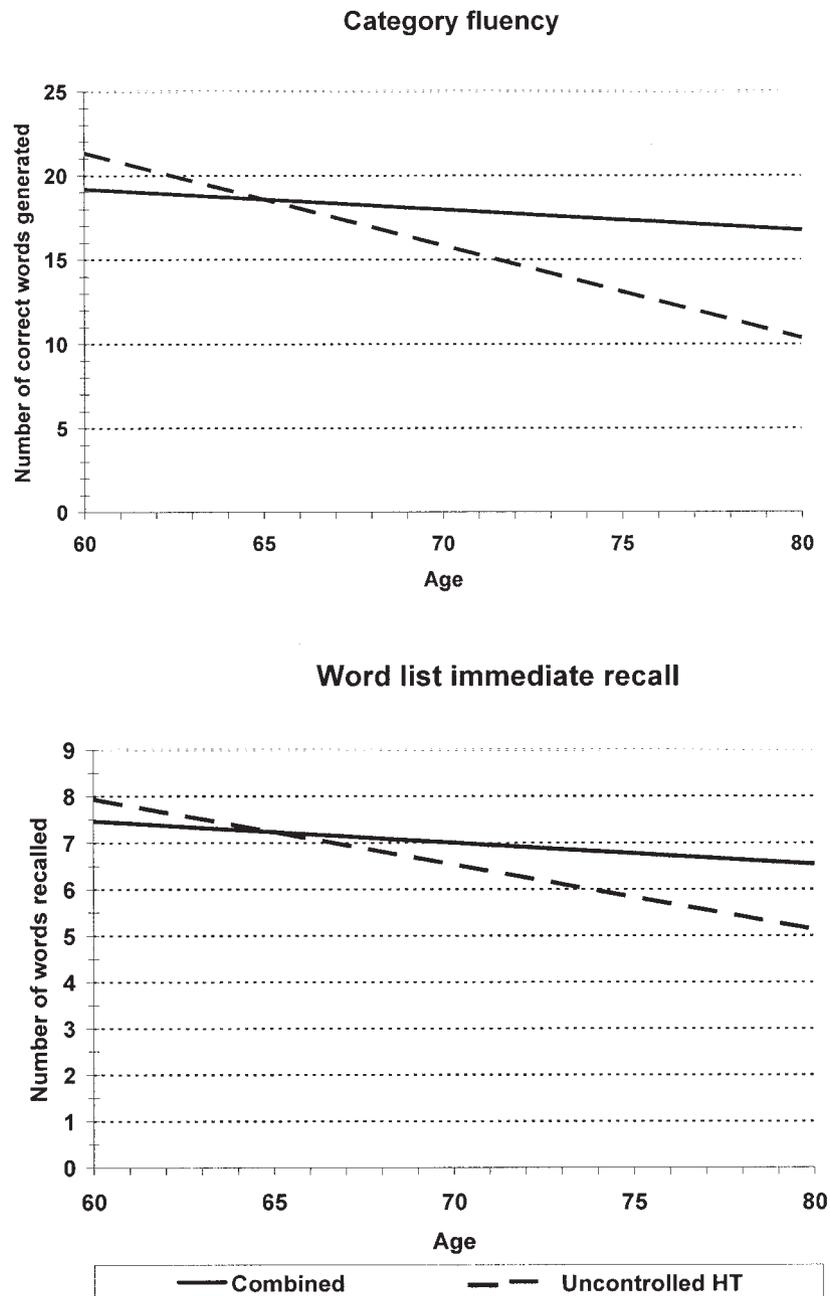


Figure 1. Upper panel: Predicted category fluency performance as a function of age for uncontrolled hypertensives (HTs; dotted line) versus the combined (solid line; i.e., normotensives, controlled and untreated HTs) group. Lower panel: Predicted word list immediate recall performance as a function of age for uncontrolled HTs versus the combined group.

group. By age 80, there was about a 7.0-word difference in generation performance between the two groups. Similarly, the lower panel of Figure 1 shows the increasing immediate recall age differences for the uncontrolled hypertensives relative to the combined group, with an approximate 1.5-word recall difference between the groups by age 80. Therefore, with increasing age, neither high blood pressure nor treatment for hypertension alone affected category fluency and immediate recall performance; however, uncontrolled hypertension in older men produced deleterious effects on the ability to rapidly retrieve lexical items (i.e., exemplars) from a semantic category in the verbal fluency task and to retrieve words from memory in the word list immediate recall task. Furthermore, these deficits were greater than would be expected as a result of age alone.

In secondary analyses, we examined two models that tested whether blood pressure per se mediated the cognitive effects of hypertension status reported above. One model examined whether SBP and DBP alone (i.e., without hypertension status) predicted cognition; the other model examined whether the Age \times Hypertension Status interaction in cognition reported above remained after we covaried SBP and DBP. In each model, we separately examined blood pressure measures taken concurrently with the cognitive examination and the average blood pressure values taken over the concurrent and previous visit (i.e., over an approximately 3-year interval). In these models, we included more extensive measures of SBP and DBP (average of sitting [both arms], standing [right arm], and supine [right arm] readings) and controlled for age and education. No blood pressure measure was significant in any of the analyses.

Discussion

We examined the following question: Do age effects on cognition vary as a function of hypertensive status? The answer is, yes. Age was negatively related to performance on all of the cognitive tests (except Digit Span Backward), and there was an interaction between age and hypertensive status for category fluency and word list immediate recall performance. In particular, with increasing age, uncontrolled hypertensives exhibited significantly larger decrements on category fluency (2.4 times greater) and immediate recall (1.3 times greater), compared with normotensives. Knowledge of our participants' clinically defined blood pressure and hypertension treatment status allowed us to more accurately delineate the effects on cognition of age from those of hypertension. Furthermore, these findings show that these age-hypertension status-cognition relations were complex.

These results are comparable to those of a recent study (Alves de Moraes, Szklo, Knopman, & Sato, 2002) that found an analogous Age \times Hypertensive Status interaction in which, relative to normotensives, older uncontrolled hypertensives exhibited larger age differences on the Digit Symbol Substitution Test (Wechsler, 1981); however, this interaction was not seen in delayed word recall or letter fluency performance. There are several differences between our study and Alves de Moraes et al.'s that preclude a direct comparison of results; namely, differences in the tests (e.g., category fluency vs. letter fluency, respectively), the 6-year interval that they used to define stable hypertensive status, their different hypertensive status definition (e.g., their uncontrolled hypertensives appeared to consist of both treated and untreated hyper-

tensives), the younger age of their sample (48–67 years old), and their inclusion of participants with medical comorbidities. Regardless, the findings from the present study, Alves de Moraes et al., and others (e.g., Waldstein, Brown, Maier, & Katzel, 2005; Waldstein & Katzel, 2001) all suggest that older adults with uncontrolled hypertension exhibit specific cognitive deficits beyond those attributable to age alone. Taken together, these recent findings in uncontrolled hypertensives are novel in the otherwise extensive literature on blood pressure effects on cognition.

The pattern of performance on category fluency and immediate recall in the present study suggests that older uncontrolled hypertensives may exhibit larger age differences on tests that require more demanding retrieval processes. For example, category fluency requires participants to quickly retrieve lexical items (i.e., exemplars) from a semantic category, and research has shown that retrieval strategies that enhance fluency performance decline with age (e.g., Troyer, Moscovitch, & Winocur, 1997). Furthermore, immediate recall from memory is more dependent on retrieval processes than are cued recall or recognition, and larger age differences are seen in recall measures (e.g., Schonfield & Robertson, 1966). Because such retrieval processes are thought to be mediated by frontal systems (e.g., Moscovitch & Winocur, 1992; Stuss & Benson, 1986; Troyer, Moscovitch, Winocur, Alexander, & Stuss, 1998) and because it has been suggested that aging is associated with increased frontal system dysfunction (e.g., Dempster, 1992; West, 1996), perhaps uncontrolled hypertension exacerbates age effects on certain frontally mediated retrieval processes. Accordingly, studies (Klungle et al., 2000, 1999; Liao et al., 1996) have shown that people with poorly controlled hypertension have greater amounts of white matter lesions on structural MRI, and Raz et al. (2003) have recently shown that hypertensives have reduced prefrontal cortex and underlying white matter volumes, with concomitant frontally mediated cognitive dysfunction. Given the importance of white matter tracts in connections between the frontal lobes and cortical and subcortical structures (e.g., Cummings, 1993), the role of hypertension and other vascular disease risk factors (e.g., Brady et al., 2001) should be considered more extensively in studies of age-related frontal system dysfunction.

We also found that there were no differences in cognition among the normotensive and the controlled and untreated hypertensive groups. The similar cognitive profiles in the normotensives and controlled hypertensives, groups that had equivalent blood pressure, suggests that antihypertensive medications did not have a negative effect on cognition, which is consistent with some previous studies (e.g., P. Nilsson, Gullberg, Ekesbo, Von Schenck, & Gustafson, 1998; Prince, 1997; Schultz et al., 1989; Starr, Whalley, & Deary, 1996). Although somewhat surprising, the lack of differences in cognition between the normotensives and untreated hypertensives is consistent with other studies that found no relation between blood pressure and cognition (e.g., Farmer et al., 1987); however, many studies have found otherwise (e.g., M. F. Elias, D'Agostino, Elias, & Wolf, 1995; M. F. Elias et al., 1998; Waldstein, Ryan, Manuck, Parkinson, & Bromet, 1991). Such inconsistencies among studies of hypertension and cognition are likely due to differences in the ages of the samples, cognitive measures, definitions of hypertension, chronicity and severity of

hypertension, time interval between hypertension diagnosis and cognitive examination, and health (e.g., comorbidities) of the samples used.

Knowing the hypertensive status of participant samples in cognitive aging research provides important additional information about the potential etiology of age-related cognitive dysfunction. The present results and those of previous studies (e.g., Alves de Moraes et al., 2002; Anstey & Christensen, 2000; M. F. Elias et al., 1998; M. F. Elias, Robbins, Schultz, & Pierce, 1990; Madden & Blumenthal, 1998; Raz et al., 2003; Waldstein et al., 2005) illustrate the need for better understanding the role of hypertension, its treatment, and health more generally in delineating "normal" cognitive aging. Despite these findings, the role of health effects on age differences in cognitive domains continues to be underappreciated in much of the cognitive aging literature. Because cognitive aging studies frequently use self-report health measures, which may inaccurately estimate medical health (see L.-G. Nilsson et al., 1997), future studies would benefit from the inclusion of more objective measures to assess health effects on age-cognition relations (see also Anstey & Christensen, 2000). Furthermore, because some vascular disease risk factors, such as hypertension, can be treated effectively, cognitive decline related to these risk factors, and vascular disease per se, may be prevented or its course modified through more aggressive treatment and improved compliance (e.g., Gorelick, 1997).

There are several limitations to the present study. First, this was a male and primarily Caucasian sample; thus, the present results do not provide information about whether the hypertension effects seen in this study are present in women or minorities. Second, the test battery given by the NAS was designed as a relatively brief general assessment of cognition. The battery was not designed to provide a thorough assessment of specific cognitive domains, and, therefore, the present results should be confirmed and further elucidated in future studies that use a more detailed, complete neuropsychological battery. Third, our dementia screening was not state of the art; however, we believe that it was at least as thorough as those conducted in many cognitive aging studies. Finally, although our overall sample was relatively large, some of the non-significant results may have been due to the relatively smaller sizes of hypertensive subsamples. Future research should sample larger numbers of persons with controlled, untreated, and uncontrolled hypertension to confirm the present results.

Despite the limitations described above, our older adult sample was medically well characterized, to a degree not commonly seen in the general cognitive aging literature. Given that our hypertensive participant sample was free of medical comorbidities, these results are less prone to confounds related to these comorbidities. Therefore, we were able to delineate specific effects of aging and hypertension on cognition. Accordingly, the effects in this study may underestimate the effects of uncontrolled hypertension on cognition in the less healthy general older adult population. Because a large proportion (37%) of older adults have uncontrolled hypertension and, furthermore, because hypertension prevalence increases, whereas hypertension control decreases, with increasing age, a substantial proportion of older adults may exhibit exacerbated age-related cognitive deficits that may be underrecognized in both research and clinical settings.

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