



Published in final edited form as:

Clin Gerontol. 2013 ; 36(2): 113–131. doi:10.1080/07317115.2012.749322.

A Comparison of Cognitive and Everyday Functional Performance among Older Adults With and Without Hypertension

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Abstract

Secondary data analyses examined the differences in cognitive and instrumental activities of daily living (IADL) performance among hypertensive individuals taking one of four classes of antihypertensive medications, hypertensive individuals not taking any antihypertensive medications, and normotensive individuals (N=770). After adjusting for covariates, significant group differences were evident on all measures (speed of processing, motor speed, reaction time, $ps < .05$) except memory and Timed IADL ($ps > .05$). Follow-up a priori planned comparisons compared hypertensive individuals not on medications to each of the four antihypertensive medication groups. Results indicated that only those on beta blockers (BB) were significantly slower in speed of processing ($ps < .05$). A priori planned comparisons also revealed that normotensive individuals had better cognitive performance on measures of processing speed, motor speed, and reaction time than hypertensive individuals regardless of antihypertensive medication use. Additionally, normotensive individuals performed significantly better on memory (Digit and Spatial Span) than individuals with hypertension on medications. No differences were found between groups on memory (Hopkins Verbal Learning Test) or Timed IADL performance. With regard to antihypertensive medications, the use of BBs was associated with slowed processing speed. These analyses provide empirical evidence that hypertension primarily impacts speed of processing, but not severe enough to affect IADL performance. Given the contribution of processing speed to memory and executive function performance, this is an important finding. Clinicians need to take into consideration the potential negative impact that BBs may have on cognition when determining the best treatment of hypertension among older adult patients.

Keywords

Hypertension; antihypertensive medications; instrumental activities of daily living; speed of processing; older adults

Hypertension is a chronic condition defined as a persistent systolic blood pressure greater than 140 mm Hg and/or diastolic blood pressure greater than 90 mm Hg (Keenan & Rosendorf, 2011). Hypertension negatively affects many parts of the body (Beevers, Lip, &

O'Brian, 2001; Calhoun et al., 2008) including the brain. Evidence from a population-based cohort study of 20 year follow-up suggests that untreated hypertension was the strongest predictor for an increased risk of dementia and cognitive decline (Kilander, Nyman, Boberg, Hansson, & Lithell, 1998). Longitudinal studies have also suggested that hypertension in midlife is associated with cognitive impairment later in life (Amenta, Mignini, Rabbia, & Tomassoni, 2002). However, it is unclear if antihypertensive medications for hypertension alleviate these cognitive declines.

There is evidence that hypertension has an adverse impact of cognitive abilities such as executive function, speed of processing, and memory (Saxby, Harrington, McKeith, Ford, & Wesnes, 2003; Tanaka & Cartez-Cooper, 2008). Older adults with uncontrolled elevated blood pressure have greater cognitive decline over six-years as compared to normotensive individuals (Alves de Moaes, Szklo, Knopman, & Sato, 2002). However, the extent to which treatment reduces the cognitive impact of hypertension is unclear (Raz, Rodrigue, & Acker, 2003). Limited evidence suggests that those with pharmacologically-treated hypertension may have less risk for cognitive decline than those untreated, unsuccessfully treated, or without hypertension (Dufouil et al., 2001; Fukuda & Kitani, 1995; Tzourio, Dufouil, Ducimetriere, & Alperovitch, 1999). Although studies indicate that certain antihypertensive medications may positively affect cognitive functioning (Amenta et al., 2002; Muldoon et al., 2002; Papademetriou, 2005), it is still unclear as to which class of antihypertensive medications have an impact, and on what cognitive functions.

The Disablement Process (Verbrugge & Jette, 1994) describes the impact that factors such as health, disease, and cognition have on functional impairment. According to this model, the presence of a chronic disease often leads to cognitive impairment, which will then lead to subsequent functional limitations, and eventually disability. Chronic conditions can negatively affect Instrumental Activities of Daily Living (IADL) performance. Therefore, according to the disablement process, it is likely that older adults with hypertension may have cognitive impairments that lead to impaired IADL performance. Similarly, according to the competency perspective (Berg, 2008), IADL performance is dependent on cognition. Thus the cognitive deficits associated with hypertension and antihypertensive medications described above could further result in IADL difficulties. However, to our knowledge no studies have examined these relationships using performance-based measures of IADLs. Therefore, this study examines whether there are any differences in cognitive and IADL performance among hypertensive individuals (with and without the use of antihypertensive medications) and normotensive individuals among a large community-based sample of older adults.

Antihypertensive Medications and Cognition

Cardio-selective medications such as angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB) and beta blockers (BB) are considered life-sustaining drugs because they can prevent remodeling of the heart and reduce mortality and morbidity (Ong, 2009; Skoog et al., 2005). Animal studies suggest that ACE inhibitors may have a protective effect on cognition (Gard, 2008). However, the effects of either ACE inhibitors or ARBs on cognition have been controversial (Manns et al., 2011). Recent evidence suggests

that the renin angiotension system plays a central role in linking hypertension to cognitive function (Hajjar et al., 2012). There is increasing evidence that inhibition of the renin angiotension system with ACE and ARB treatment may provide end-organ protection independent of blood pressure lowering. However, the effects of such treatment on cognition are inconclusive (Kehoe & Wilcock, 2007).

A study by Muldoon and colleagues (2002) was the first to experimentally compare different types of antihypertensive drug classes [lipophilic and hydrophilic BB, a thiazide diuretic, a centrally-acting alpha-agonist (CAA), a calcium channel blocker (CCB), and an ACE inhibitor] using a double-blind cross-over design after two weeks of washout period among individuals 25–55 years of age. This study found that regardless of medication type, treatment slowed completion on the Trail Making Test and reduced simple motor speed on the Finger Tapping Test. The effects of the medications on memory were mixed. All antihypertensive agents positively impacted immediate recall, but diminished performance on delayed recall of word pairs. Both CAA and BB reduced motor speed, but otherwise there was a general absence of drug-specific effects on cognitive function. Muldoon and colleagues (2002) concluded that any effects from antihypertensive medications will be small and would not impact a person's everyday activities. However, performance of IADL was not measured and the effects of medications may differ for an older adult population (65+).

A review of studies on the effects of antihypertensive medications conducted by Fournier and colleagues (2009) indicated that CCBs and ARB were protective against cognitive decline, while BB's and CAA's negatively impacted cognition. Saxby and colleagues (2008) found that older adults taking ARB's may be less susceptible to cognitive decline as measured by reaction time and memory. In addition, the cardiovascular health study showed that the ACE inhibitors may slow cognitive decline (as measured by mental status) compared with other antihypertensive medications. Protective effects of CCBs were evident in a study conducted by Hanon and colleagues (2006) in which CCB use was associated with better Mini-Mental State Examination (MMSE) scores and a composite of cognitive efficiency among a sample of older adults. In contrast, non-centrally active ACE inhibitors were associated with greater risk of dementia and self-reported IADL impairment (Sink et al., 2009)

There are several limitations to these studies. First, most used measures of mental status, which do not indicate the particular aspect(s) of cognition impacted by antihypertensive medication use. IADL impairment, when included, was measured by self-report rather than a performance-based measure, which may be more sensitive and show differing results. Finally, individual characteristics associated with both cardiovascular health and cognition were not controlled for and could have confounded results (Seux et al., 1998; Zieman, Schulman, & Fleg, 2003).

Previous research has demonstrated that age (Zieman et al., 2003), number of depressive symptoms (Steffens, Krishnan, Crump, & Burke, 2002), and education (Bennett et al., 2003; Seux et al., 1998), are associated with both cardiovascular health and cognition, and thus need to be statistically considered when cognitive function is the outcome variable of

interest. Differences in how these variables are accounted for may be a contributing factor to the discrepant findings in the antihypertensive medication literature.

Hypertension and Everyday Cognitive Performance

Research examining the effects of hypertension and antihypertensive medications on IADL is limited. Although Dodge and colleagues (2005) found that hypertension was not associated with self-reported IADL impairment, others found that hypertension was associated with increased IADL difficulty, also measured by self-report (Wang, van Belle, Kukull, & Larson, 2002). Sink et al. (2009) found that ACE inhibitors were associated with IADL impairments, but again, this was by self-report. To our knowledge, no studies have examined the effect of hypertension or antihypertensive medications on actual IADL *performance*. If hypertension negatively impacts cognition, such cognitive difficulties may further result in IADL impairment.

Purpose

The purpose of these secondary data analyses was to compare memory, processing speed, motor speed, reaction time, and actual IADL performance among a community-based sample including both hypertensive (with and without antihypertensive medication use) and normotensive older adults while controlling for factors that may impact cognition. An emphasis on speed of processing measures was included due to the importance of this ability in relationship to IADL performance (Owsley, Sloane, McGwin Jr., & Ball, 2001), as well as the overlapping contributions of cognitive speed of processing to memory and executive functioning (Verhaeghen, 2011), which are more commonly examined in relation to hypertension. Secondary data analyses were conducted on cognitive data from an existing study of aging and cognition. Six groups of older adults were compared: those without hypertension, those with hypertension not taking medications, and those with hypertension treated with an ACE, ARB, BB, CAA, or alpha blocker (AB).

Method

Participants

Analyses included 770 participants of the Staying Keen in Later Life (SKILL) dataset who completed baseline assessments. The SKILL study was designed to examine cognitive and functional abilities among a large sample of community-dwelling older adults. Secondary data analyses were conducted to begin to investigate whether there are differences in cognitive and IADL performance among those with self-reported hypertension, who were and were not taking antihypertensive medications, and normotensive individuals. Ages ranged from 62.00 to 97.73 years with a mean of 73.28 years ($SD = 5.87$ years) and education levels ranged from six to 20 years with a mean of 13.99 years ($SD = 2.67$). The participants included 466 (60.5%) females and 304 (39.5%) males. In the sample, 686 (89.3%) participants reported being Caucasian Americans and 77 (10.0%) participants reported their race as African American. Of the 770 participants, 390 (50.6%) self-reported hypertension, of whom 222 also reported antihypertensive medication use. Of those taking antihypertensive medications, 115 were taking an ACE inhibitor, 47 were taking ARB, 42

were taking a BB, and 18 were taking an AB. Only six reported taking CAA, and due to the small sample size were excluded from analyses. 168 participants reported hypertension, but were not taking any medications for treatment, and 380 participants reported not having hypertension and were not taking any antihypertensive medications. Participants who reported taking more than one antihypertensive medication (n=69) were not included in analyses due to the inability to distinguish the effects of one antihypertensive medication from another.

Measures

Health and Hypertensive Status—Research assistants asked participants about their medical history. Participants responded by answering “yes” “no” or “do not” know” to questions pertaining to visual and general health using a previously validated questionnaire (Jobe et al., 2001). Each question began, “Has a doctor or nurse ever told you that you have...” and then general health condition was named including: arthritis; asthma and/or other breathing problems; cancer; chronic skin problems; diabetes; heart disease; heart problems other than heart disease; high cholesterol; hypertension; mood problems such as depression or anxiety; multiple sclerosis; osteoporosis; Parkinson’s disease; Stroke, mini stroke, or TIA; and any other significant health conditions. An individual was categorized as hypertensive based on an affirmative response to, “Has a doctor or nurse ever told you that you have hypertension or high blood pressure?” Thus, hypertension status was self-reported.

Memory—The WMS-III Digit Span and Spatial Span (Wechsler, 1999) measures were used to evaluate verbal and non-verbal attention and short-term memory. Digit Span requires participants to repeat a string of verbally presented digits. Similarly, during the Spatial Span subtest, the examiner taps a sequence on fixed blocks and the participant repeats the sequence. Total correct was recorded for each measure.

The Hopkins Verbal Learning Test (HVLT) (Brandt, 1991) involves a list of 12 words that fit into three different semantic categories. Part A of the HVLT required participants to listen to a list of words and immediately recall them. Three trials were completed and the total number of words correctly recalled from each trial was used in analyses. Higher scores indicate better immediate recall.

Speed of Processing—The Trail Making Test (Reitan & Wolfson, 1985) is composed of two parts, A and B, with the latter considered a measure of mental set flexibility. Trails A require participants to sequentially connect a series of 25 numbered circles as quickly as possible. Trails B require participants to sequentially connect a series of 25 circles by alternating between numbers and letters (i.e., 1-A-2-B-3-C). Time to completion was recorded and was limited to 480 s in this study (Wood et al., 2005).

The Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Substitution Test (DSST; Wechsler, 1981) requires participants to reference a symbol-number key and fill in the appropriate symbols based on the number provided. Participants have 90 seconds to work on the task. Total number correct was recorded.

The computerized UFOV[®] test measures cognitive processing speed and assesses the minimum display duration needed for the participant to attend to multiple visual stimuli (Edwards et al., 2006). This test is comprised of four subtests that measure speed of processing under increasing demand and require the participant to identify and localize targets with presentation lengths ranging between 17 and 500 ms. For each subtest, the 75% threshold is quantified (Edwards et al., 2006).

Letter Comparison (Salthouse & Babcock, 1991) requires participants to determine whether sets of letters are identical. For each set size (three, six, or nine letters), participants complete as many comparisons as possible in the time allotted. All three scores are summed to total the number correct.

Similar to Letter Comparison, Pattern Comparison (Salthouse & Babcock, 1991) uses line segments as the stimulus rather than letters. As before, complexity level varies by the number of line segments presented (three, six, or nine lines). The number of correct trials was summed for the total score.

Reaction Time—The Road Sign Test is a computerized measure of complex reaction time (Ball et al., 2002; Ball & Owsley, 2000; Edwards et al., 2005). After successful learning trials, participants are presented with groups of three or six stimuli, only one of which requires a response. The stimuli consist of road signs (pedestrian, bicycle, right and left turn arrows) with and without a red slash through them. If the sign does not have a red slash through it, the participants react in one of three ways. For the bicycle and pedestrian signs, the participant is required to press the button on a computer mouse as quickly as possible. When a participant is presented with a right or left arrow, they are required to move the mouse in the direction indicated by the arrow as quickly as possible. Participants are instructed to ignore any sign that has a red slash through it. The number of stimuli presented and the location of the signs can vary. Time to respond was recorded, and the average response time was used for analyses.

Motor Speed—Digit Symbol Copy (DSC; Tun, Wingfield, & Lindfield, 1997) requires participants to fill in a grid of empty squares with the exact symbols presented above each square. Unlike Digit Symbol Substitution in which participants had a set time (90 seconds) to complete as many items as possible, participants were timed to see how fast they could complete the entire page. They were instructed to work as quickly as possible and the average number of seconds per item was calculated and used for analyses (Edwards et al., 2005).

Timed IADL—The Timed IADL test (Kovar & Lawton, 1994; Owsley et al., 2001) consists of five timed tasks representing common everyday activities of daily living involving searching for and processing information. Activities include looking up a name in the telephone book, counting out correct change, reading the directions on medicine containers, locating and reading the ingredients on food can labels, and locating items on a shelf full of food. Except for the telephone task (three minutes), each task has a time limit of two minutes. Time (in seconds) required and accuracy of each task was recorded. Summary z-scores are used in analyses as detailed by Owsley and colleagues (Owsley et al., 2001).

Covariates—Age in years, education in years, far visual acuity, and number of depressive symptoms as measured by the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), were explored as covariates because these factors are often associated with cognitive and cardiovascular health in older adults (Seux et al., 1998; Ziemann et al., 2003). Far visual acuity was measured with glasses, if worn, and without glasses, if not worn for distance. A standard ETDRS chart with a Good-Lite Model 600A light box was used to measure far visual acuity. The number of correctly identified letters on the chart determined the score on a scale of 0 to 90. The CES-D measures depressive symptoms. This 12 question, self-administered instrument assesses the frequency of symptoms during the past week. Total number of endorsed items was used for this analysis.

Procedure

The study included community-dwelling older adults from Bowling Green, KY, Birmingham, AL, and surrounding areas who were recruited by mass-mailed information letters. Some participants were referred by other research participants or had been previously screened for university-affiliated research projects (Wood et al., 2005). The recruitment methods for this study are detailed elsewhere (Edwards et al., 2005; Wood et al., 2005). Older adults completed a 1.5 hour screening visit that determined eligibility. Eligibility criteria included: age equal to or greater than 60 years, minimum far visual acuity score of 20/80 (with use of corrective lenses if needed), and a fifth grade literacy level. Eligible participants completed a 2.5-hour baseline visit assessing sensory, cognitive, and functional abilities (Wood et al., 2005). Medical history, including history of hypertension and use of antihypertensive medications, was collected at this time.

Analyses

Standardized *z*-scores were calculated from this sample for all cognitive outcome variables so that all measures would be on the same scale. The SKILL sample was very diverse in cognitive function due to the limited exclusion criteria. To minimize the impact of outliers, such scores were re-coded to ± 2.5 standard deviations from the mean. This method of handling outliers has been used in prior analyses of SKILL data (Edwards et al., 2005). MANOVA was first used to compare the six groups (ACE, ARB, AB, BB, hypertension-without-medication, and normotensive individuals) on the potential covariates (age, education, far visual acuity, and number of depressive symptoms). Any covariate indicating potential group differences at an alpha level of .10 or less was included in subsequent analyses. Second, MANCOVA was used to compare these six groups on speed of processing, motor speed, reaction time, memory, and Timed IADL while adjusting for significant covariates. Follow-up analyses were conducted using univariate ANOVAs for each outcome measure. A priori planned comparisons were used to compare those with hypertension and not on medications to each of the four antihypertensive treatments to examine whether there were differences between these groups in cognitive or IADL performance. Those with hypertension not on medications and normotensive individuals were also compared to those with hypertension taking an antihypertensive medication. An alpha level of .05 was considered statistically significant for analyses examining hypotheses.

Results

The distribution of data was checked for outliers. Less than 3% of the data points were identified as legitimate outliers. As previously done with the SKILL data, (Edwards et al., 2005) these scores were recoded to $\pm 2.5 z$ to minimize the effect of extreme scores on results (Osborne & Overbay, 2004). With regard to the health of the sample, the most common health conditions reported besides hypertension (50.1%), included arthritis (60.5%) and high cholesterol (48.6%).

When MANOVA was used to compare the six groups (normotensive, hypertension no medications, and hypertension taking an ACE, ARB, AB, or BB) across age, education, far visual acuity, number of depressive symptoms, number of health conditions (other than hypertension) results indicated an overall difference, Wilks' $\Lambda = .902$, $F(25, 2824) = 3.19$, $p < .001$, partial $\eta^2 = 0.02$. Univariate analyses indicated that the groups significantly differed in number of depressive symptoms $F(5, 764) = 2.93$, $p = .013$, partial $\eta^2 = .019$, and number of health conditions (other than hypertension) $F(5, 764) = 9.86$, $p < .001$, partial $\eta^2 = .061$. Marginal group differences were found for age, $F(5, 764) = 2.14$, $p = .059$, partial $\eta^2 = .014$. Group differences in education, $F(5, 764) = 1.21$, $p = .302$, partial $\eta^2 = .008$, and far visual acuity $F(5, 764) = 1.84$, $p = .103$, partial $\eta^2 = .012$ -were not significant. Means and standard deviations by group are reported in Table 1.

Age, number of depressive symptoms, and total number of health conditions (other than hypertension) were used as covariates in subsequent analyses. MANCOVA to compare the six groups across cognitive measures revealed an overall group difference, Wilks' $\Lambda = .899$, $F(60, 3515) = 1.35$, $p = .040$, partial $\eta^2 = 0.21$. Univariate ANCOVAs revealed that age significantly impacted performance on all cognitive tasks ($ps < .01$). Depressive symptoms significantly impacted performance on all cognitive tasks ($ps < .05$) except for Digit Span ($p = .11$). After adjusting for age, number of depressive symptoms, and total number of health conditions (other than hypertension) significant group differences were evident on all tasks ($ps < .05$) except HVL, Digit Span, Spatial Span, and Timed IADL ($ps > .05$). Means and standard deviations of the groups are reported in Table 2.

A priori planned comparisons were performed on the adjusted measures, comparing those with hypertension not on medications to each of the four antihypertensive medication groups. Among those with hypertension, there were no relationships of any antihypertensive medications with the exception of BB. Those on BB performed worse on three of the processing speed measures (Letter Comparison, Trail Making Test A and B), and had slower motor speed (Digit-Symbol Copy) than those with hypertension who were not taking medications ($ps < .05$).

Individuals with hypertension not on medications were compared to normotensive individuals. Normotensive individuals performed better on most of the processing speed measures (Trail Making Test A and B, UFOV, Pattern Comparison, Digit Symbol Substitution), as well as motor speed (Digit-Symbol Copy) and reaction time (Road Sign Test) ($ps < .02$).

Normotensive individuals were also compared to those with hypertension taking any type of antihypertensive medications. Similar to those with hypertension not on medications, normotensive individuals performed better on motor speed, reaction time, and the same measures of speed of processing than those with hypertension on medications (collapsed across treatments) ($ps < .01$). In contrast, normotensive individuals also performed significantly better on memory (Digit and Spatial Span) and one additional measure of processing speed (Letter Comparison) than individuals with hypertension on medications. No differences were found between any of the groups on the HVLT or Timed IADL performance ($ps > .05$). Thus normotensive individuals had better cognitive performance on measures of processing speed, motor speed, and reaction time than hypertensive individuals (both with and without medications). However, individuals on antihypertensive medications also performed significantly worse than normotensives in memory performance.

Discussion

Analyses were conducted to compare memory, processing speed, motor speed, reaction time, and IADL performance among a community-based sample including hypertensive (with and without antihypertensive medication use) and normotensive older adults while controlling for other factors that may impact cognition. Our results indicate that sample characteristics (i.e., age, number of depressive symptoms, and number of other health conditions) were significantly related to cognitive performance and differed among those with and without hypertension. Individuals with hypertension (both with and without antihypertensive medication) had more depressive symptoms and reported a greater number of other health conditions. When age, number of depressive symptoms, and number of other health conditions were controlled, individuals with hypertension, regardless of medication use, demonstrated poorer performance on measures of processing speed, reaction time, and motor speed than normotensive individuals. With regard to memory, there were only differences between normotensive individuals and those with hypertension taking antihypertensive medications on Digit and Spatial Span. However, no differences with respect to IADL performance were observed when adjusting for covariates. Owsley and colleagues demonstrated that Timed IADL performance was strongly related to cognitive speed of processing (Owsley et al., 2001). Although hypertension was associated with slower speed of processing, these cognitive difficulties may not be severe enough to affect IADL performance.

Results support the hypothesis that individuals with hypertension have poorer cognitive functioning in some domains than normotensive individuals. Hypertensive individuals, regardless of whether they were on antihypertensive medications, performed more poorly on measures of motor speed, reaction time, and speed of processing. Although there were no differences between those with and without hypertension on IADL performance, interestingly, individuals with hypertension performed worse on the UFOV, which has demonstrated predictive validity for motor vehicle collisions in older adults (Ball et al., 2005). Further research should examine if this population is at increased risk for adverse driving events.

Contrary to prior evidence that antihypertensive medications *positively* impact cognition, hypertensive individuals on antihypertensive medications performed significantly worse than normotensive individuals on memory performance. Whereas those individuals with hypertension who were not taking medications performed the same on memory tasks as normotensive individuals.

While Muldoon and colleagues (2002) found that antihypertensive agents positively impacted memory performance among those aged 25–55, we did not find the same results among our participants who were 65 years and older after adjusting for covariates. Similar to the results of Muldoon and colleagues (2002), in the present study individuals with hypertension taking a BB were more likely to experience slower motor speed and speed of processing. The present study also provides empirical support for the assertion of Muldoon and colleagues that cognitive difficulties associated with hypertension are not severe enough to impact IADL performance.

There are limitations to this study that should be noted. Although the present study was the first to look at the relationship of four different antihypertensive medications on cognitive and everyday functioning among older adults, the sample size of hypertensive individuals taking ARBs was small. In addition, even though this study focused primarily on antihypertensive medications, actual blood pressure measurements are obviously preferred over self-report. Although this would not likely change our results, it would improve internal validity for the study. The cognitive battery had a heavy emphasis on processing speed and attention, with little inclusion of other cognitive abilities such as language, executive functioning, or visuospatial skills. Another limitation to the study is the absence of a delayed recall memory component. Although there were few group differences in immediate memory, examining delayed recall may reveal different results. Even so, the cognitive battery in the SKILL study was more extensive than that of prior studies examining hypertension and cognition, and the emphasis on speed of processing is important given the overlapping contributions of this cognitive ability to memory and executive function (Verhaeghen, 2011), which are more commonly examined. Another limitation is that the measure used to assess IADL performance only assesses five domains. The Timed IADL was designed to assess rapid and efficient performance of tasks beneficial to daily life from the established IADL domains of telephone communication, financial abilities, nutrition, shopping, and medication usage (Owsley, Sloane, McGwin, & Ball, 2002). This measure has shown construct validity in comparison to other well-accepted measures of everyday function (Gross, Rebok, Unverzagt, Willis, & Brandt, 2011). Unfortunately, measures of everyday functional performance are somewhat limited.

The relationships found in this study suggest that hypertension may negatively affect areas of the brain related to speed of processing, reaction time, and motor speed. According to Raz and colleagues (2003), chronically elevated blood pressure increases the likelihood of structural brain abnormalities. Furthermore, they found that individuals with hypertension had a smaller prefrontal cortex, underlying white matter volumes, and increased frontal white-matter hyperintensities as compared to those without hypertension (Raz et al., 2003). Further research needs to investigate the underlying causes of cognitive decline among those with hypertension, regardless of medication use. Given that speed of processing, reaction

time, and motor speed are linked to prefrontal cortex functioning, which has been shown to be affected by both aging and hypertension (Raz et al., 2003), an interesting area for future research would be to explore the impact that BB have on the prefrontal cortex. This study adds to the growing evidence that hypertension is primarily related to the cognitive domain of processing speed, and that of the antihypertensive medications, use of BB in particular is associated with slowed processing speed. With the addition of this study to the current literature, it is becoming clear that studies of aging and cognition need to consider the role of hypertension as well.

Clinicians need to be knowledgeable about the type of antihypertensive medication prescribed to older adult patients. In addition to health factors (e.g. age, how high the blood pressure is, and whether the patient has any organ damage), clinicians need to consider that some antihypertensive medications may negatively affect cognition (Gliebus, 2007). According to our findings, BBs may have the greatest adverse impact, specifically on speed of processing, in comparison with ABs, ARBs, and ACE inhibitors. The negative associations with cognition may be due to the decreased arterial blood pressure and reduced cardiac output of BBs. This often causes dizziness due to hypoperfusion to the brain, which may be causing the observed deficits in speed of processing (Klabundy, 2011). Thus, BBs may not be the preferred choice in the treatment of primary hypertension among older adults (Lindholm, Carlberg, & Samuelson, 2005). Older adults' awareness of cognitive difficulties, particularly in speed of processing, may be limited. Thus clinicians need to take into consideration the potential negative impact that BBs may have on cognition, specifically speed of processing, compared to other classes of antihypertensive medications when determining the best treatment of hypertension among older adult patients.

Acknowledgments

This work was supported by the National Institutes of Health/National Institute on Aging Grants I P30 AG022838-01-Edward R. Roybal Center for Translational Research on Aging and Mobility- and 5 R37 AG05739-16-Improvement of Visual Processing in Older Adults, Karlene K. Ball, principal investigator. The authors would like to thank Dr. Karlene Ball and all the research assistants, graduate students, and staff of Western Kentucky University and the University of Alabama at Birmingham Edward R. Roybal Center for Translational Research on Aging and Mobility for their assistance in data collection for the SKILL studies.

References

- Alves de Moaes S, Szklo M, Knopman D, Sato R. The relationship between temporal changes in blood pressure and changes in cognitive function: Artherosclerosis risk in communities (ARIC) study. *Preventative Medicine*. 2002; 35:258–263.10.1006/pmed.2002.1007
- Amenta F, Mignini F, Rabbia F, Tomassoni D. Protective effect of antihypertensive treatment on cognitive function in essential hypertension: Analysis of published clinical data. *Journal of the Neurological Sciences*, 203–204. 2002:147–151.10.1016/S0022-510X(02)00281-2
- Ball K, Berch DB, Helmers KF, Jobe JB, Leveck MD, Marsiske M, Unverzagt FW. Effects of cognitive training interventions with older adults. A randomized controlled trial. *JAMA*. 2002; 288:2271–2281.10.1001/jama.288.18.2271 [PubMed: 12425704]
- Ball, K.; Owsley, C. Increasing mobility and reducing accidents of older drivers. In: Schaie, KW.; Pietrucha, M., editors. *Mobility and transportation in the elderly*. New York: Springer Publishing Company, Inc; 2000. p. 213-251.
- Ball K, Roenker DL, Wadley VG, Edwards JD, Roth DL, McGwin D, Dube T. Can high risk drivers be identified through performance-based measures in a department of motor vehicles setting?

- Journal of the American Geriatrics Society. 2005; 54(1):77–84.10.1111/j.1532-5415.2005.00568.x [PubMed: 16420201]
- Beevers G, Lip GY, O'Brian E. ABC of hypertension: The pathophysiology of hypertension. *British Journal of Psychiatry*. 2001; 114:797–811.10.1136/bmj.322.729.1.912
- Bennett DA, Wilson RS, Schneider JA, Evans DA, Mendes de Leon CF, Arnold SE, Bienias JL. Education modifies the relation of AD pathology to level of cognitive function in older persons. *Neurology*. 2003; 60(12):1909–1915.10.1212/01.WNL.0000069923.64550.9F [PubMed: 12821732]
- Berg, CA. Everyday problem solving in context. In: Hofer, SM.; Alwin, DF., editors. *Handbook of Cognitive Aging: Interdisciplinary Perspectives*. Los Angeles: SAGE Publications; 2008. p. 207-223.
- Brandt J. The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychology*. 1991; 5:125–142.10.1080/13854049108403297
- Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, Toto RD, Carey RM. Resistant hypertension: Diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for high blood pressure research. *Hypertension*. 2008; 51:1403–1419.10.1161/HYPERTENSIONAHA.108.189141 [PubMed: 18391085]
- Dodge HH, Kadowaki T, Hayakawa T, Yamakawa M, Sekikawa A, Ueshima H. Cognitive impairment as a strong predictor of incident disability in specific ADL-IADL tasks among community-dwelling elders: The Azuchi study. *The Gerontologist*. 2005; 45(2):222–230.10.1093/geron/45.2.222 [PubMed: 15799987]
- Dufouil C, de Kersaint-Gilly A, Besancon V, Levy C, Auffray E, Brunnereau L, Tzourio C. Longitudinal study of blood pressure and white matter hyperintensities: The EVA MRI Cohort. *Neurology*. 2001; 56:921–926. Retrieved from <http://www.neurology.org/>. [PubMed: 11294930]
- Edwards JD, Ross LA, Wadley VG, Clay OJ, Crowe M, Roenker DL, Ball KK. The useful field of view test: Normative data for older adults. *Archives of Clinical Neuropsychology*. 2006; 21:275–286.10.1016/j.acn.2006.03.001 [PubMed: 16704918]
- Edwards JD, Wadley VG, Vance DE, Wood K, Roenker DL, Ball KK. The impact of speed of processing training on cognitive and everyday performance. *Aging & Mental Health*. 2005; 9:262–271.10.1080/13607860412331336788 [PubMed: 16019280]
- Fournier A, Oprisiu-Fournier R, Serot J, Godefroy O, Achard J, Faure S, Sato N. Prevention of dementia by antihypertensive drugs: how AT1-receptor-blockers and dihydropyridines better prevent dementia in hypertensive patients than thiazides and ACE-inhibitors. *Neurotherapeutics*. 2009; 9(9):1413–1431.10.1586/ern.09.89
- Fukuda H, Kitani M. Differences between treated and untreated hypertensive subjects in the extent of periventricular hyperintensities observed on brain MRI. *Stroke*. 1995; 26:1593–1597. Retrieved from <http://stroke.ahajournals.org/>. [PubMed: 7660404]
- Gard PR. Cognitive-enhancing effects of angiotension IV. *Neuroscience*. 2008; 9(Supplement 2):S2–S15.10.1186/1471-2202-9-S2-S15
- Gliebus G. The influence of beta-blockers on delayed memory function in people with cognitive impairment. *American Journal of Alzheimers Disease and Other Dementia's*. 2007; 22(1):57–61.
- Gross AL, Rebok GW, Unverzagt FW, Willis SL, Brandt J. Cognitive predictors of everyday functioning in older adults: Results from the ACTIVE cognitive intervention trial. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*. 2011; 66B(5):557–566.10.1093/geronb/gbr033
- Hajjar I, Hart M, Chen YL, Mack W, Milberg W, Chui H, Lipsitz L. Effect of antihypertensive therapy on cognitive function in early executive cognitive impairment: A double-blind randomized clinical trial. *Archives of Internal Medicine*. 2012; 172:442–444.10.1001/archinternmed.2011.1391 [PubMed: 22412114]
- Hanon O, Pequignot R, Seux ML, Lenoir H, Bune A, Rigaud AS, Girerd X. Relationship between antihypertensive drug therapy and cognitive function in elderly hypertensive patients with memory complaints. *Journal of Hypertension*. 2006; 24:2101–2107.10.1097/01.HJH.0000244961.69985.05 [PubMed: 16957572]

- Jobe JB, Smith DM, Ball K, Tennstedt SL, Marsiske M, Willis SL, Kleinman K. ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled Clinical Trials*. 2001; 22:453–479.10.1016/S0197-2456(01)00139-8 [PubMed: 11514044]
- Keenan NL, Rosendorf KA. Prevalence of Hypertension and Controlled Hypertension --- United States, 2005–2008. *Mortality and Morbidity Weekly Report*. 2011; 60(1):94–97. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/su6001a21.htm?s_cid=su6001a21_w#tab.
- Kehoe PG, Wilcock GK. Is inhibition of the renin-angiotensin system a new treatment option for Alzheimer's disease? *Lancet Neurology*. 2007; 6:373–378.
- Kilander L, Nyman H, Boberg M, Hansson L, Lithell H. Hypertension Is Related to Cognitive Impairment: A 20-Year Follow-up of 999 Men. *Hypertension*. 1998; 31:780–786.10.1161/01.HYP.31.3.780 [PubMed: 9495261]
- Klabundy, RE. *Cardiovascular Physiology Concepts*. 2. Lippincott Williams & Wilkins; 2011.
- Kovar, M.; Lawton, M., editors. *Functional disability: Activities and instrumental activities of daily living*. Vol. 14. New York: Springer; 1994.
- Lindholm LH, Carlberg B, Samuelson O. Should β blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *The Lancet*. 2005; 366(1545):1545–1553.10.1016/S0140-6736(05)67573-3
- Manns M, Leske O, Gottfried S, Bichler Z, Lafenêtre P, Wahle P, Heuman R. Role of neuronal ras activity in adult hippocampal neurogenesis and cognition. *Frontiers in Neuroscience*. 2011; 5(18): 1–8.10.3389/fnins.2011.00018
- Muldoon M, Waldstein SR, Ryan CM, Jennings JR, Polefrone JM, Shapiro AP, Manuck SB. Effects of six anti-hypertensive medications on cognitive performance. *Journal of Hypertension*. 2002; 20:1643–1652. Retrieved from <http://journals.lww.com/jhypertension/pages/default.aspx>. [PubMed: 12172327]
- Ong HT. Are angiotensin-converting enzyme inhibitors and angiotensin receptor blockers especially useful for cardiovascular protection? *Journal of the American Board of Family Medicine*. 2009; 22(6):686–697. [PubMed: 19897698]
- Osborne JW, Overbay A. The power of outliers (and why researchers should always check for them). *Practical Assessment, Research & Evaluation*. 2004; 9(6):1–9. Retrieved from <http://PAREonline.net/getvn.asp?v=9&n=6>.
- Owsley C, Sloane M, McGwin G Jr, Ball K. Timed instrumental activities of daily living tasks: Relationship to cognitive function and everyday performance assessments in older adults. *Gerontology*. 2001; 48(4):254–265.10.1159/000058360 [PubMed: 12053117]
- Owsley C, Sloane ME, McGwin G, Ball KK. Timed instrumental activities of daily living tasks: Relationship to cognitive function and everyday performance assessments in older adults. *Gerontology*. 2002; 2002:254–265.10.1159/000058360 [PubMed: 12053117]
- Papademetriou V. Hypertension and Cognitive Function: Blood pressure regulation and cognitive function: A review of the literature. *Geriatrics*. 2005; 60:20–24. Retrieved from <http://www.biotechmedia.com/bestindex.html>. [PubMed: 15700945]
- Radloff LS. The CES-D scale: A self report depression scale for research use in the general population. *Applied Psychology Measurement*. 1977; 1(3):385–401.10.1177/014662167700100306
- Raz N, Rodrigue K, Acker J. Hypertension and the brain: Vulnerability of the prefrontal regions and executive functions. *Behavioral Neuroscience*. 2003; 117:1169–1180.10.1037/0735-7044.117.6.1169 [PubMed: 14674838]
- Reitan, RM.; Wolfson, D. *The Halstead-Reitan Neuropsychological Test Battery*. Neuropsychological Press; 1985.
- Salthouse TA, Babcock RL. Decomposing adult age differences in working memory. *Developmental Psychology*. 1991; 27:763–776.10.1037/0012-1649.27.5.763
- Saxby B, Harrington F, McKeith A, Ford G, Wesnes K. Effects of hypertension on attention, memory, and executive function in older adults. *Health Psychology*. 2003; 22:587–591.10.1037/0278-6133.22.6.587 [PubMed: 14640855]
- Saxby B, Harrington F, Wesnes KA, McKeith IG, Ford GA. Candesartan and cognitive decline in older patients with hypertension: A substudy of the SCOPE trial. *Neurology*. 2008; 70:1858–1866.10.1212/01.wnl.0000311447.85948.78 [PubMed: 18458219]

- Seux ML, Thijs L, Forette F, Staessen JA, Birkenhager WH, Bulpitt CJ. Correlates of cognitive status of old patients with isolated systolic hypertension: The Syst-Eur Vascular Dementia Project. *Journal of Hypertension*. 1998; 16:963–969. Retrieved from <http://journals.lww.com/jhypertension/pages/default.aspx>. [PubMed: 9794736]
- Sink KM, Leng X, Williamson J, Kritchevsky SB, Yaffe K, Kuller L, Goff DC Jr. Angiotensin-Converting Enzyme Inhibitors and Cognitive Decline in Older Adults With Hypertension. *Archives of Internal Medicine*. 2009; 169(13):1195–1202.10.1001/archinternmed.2009.175 [PubMed: 19597068]
- Skoog I, Lithell H, Hansson L, Elmfeldt D, Hofman A, Olofsson B, Zanchetti A. Effect of baseline cognitive function and antihypertensive treatment on cognitive and cardiovascular outcomes: Study on Cognition and Prognosis in the Elderly (SCOPE). *American Journal of Hypertension*. 2005; 18:1052–1059. [PubMed: 16109319]
- Steffens DC, Krishnan KRR, Crump C, Burke GL. Cerebrovascular Disease and Evolution of Depressive Symptoms in the Cardiovascular Health Study. *Stroke*. 2002; 33:1636–1644.10.1161/01.STR.0000018405.59799.D5 [PubMed: 12053004]
- Tanaka, H.; Cartez-Cooper, M. Exercise, hypertension, and cognition. In: Spirduso, WW.; Poon, LW.; Chodzko-Zajko, W., editors. *Exercise and its mediating effects on cognition*. Champaign, IL: Human Kinetics; 2008. p. 169-181.
- Tun PA, Wingfield A, Lindfield KC. Motor-speed baseline for the Digit-Symbol Substitution Test. *Clinical Gerontologist: The Journal of Aging and Mental Health*. 1997; 18:47–51. Retrieved from <http://www.informaworld.com/smpp/title~content=t792303983~db=all>.
- Tzourio C, Dufouil C, Ducimetriere O, Alperovitch A. Cognitive decline in individuals with high blood pressure: A longitudinal study in the elderly. EVA Study Group. *Epidemiology of vascular aging*. *Neurology*. 1999; 53:1948–1952. Retrieved from <http://www.neurology.org/>. [PubMed: 10599763]
- Verbrugge LM, Jette AM. The disablement process. *Social Science & Medicine*. 1994; 38:1–14. [PubMed: 8146699]
- Verhaeghen P. Aging and executive control: Reports of a demise greatly exaggerated. *Current Directions in Psychological Science*. 2011; 20:174–180.10.1177/0963721411408772
- Wang L, van Belle G, Kukull W, Larson E. Predictors of functional change: A longitudinal study of nondemented people aged 65 and older. *Journal of the American Geriatrics Society*. 2002; 50:1525–1534.10.1046/j.1532-5415.2002.50408.x [PubMed: 12383150]
- Wechsler, D. *Wechsler Adult Intelligence Scale-Revised Manual*. New York: Psychological Corporation; 1981.
- Wechsler, D. *Wechsler Memory Scale-Revised Manual*. San Antonio: The Psychological Corporation; 1999.
- Wood KM, Edwards JD, Clay OJ, Wadley VG, Roenker DL, Ball KK. Sensory and cognitive factors influencing functional ability in older adults. *Gerontology*. 2005; 51:131–141.10.1159/000082199 [PubMed: 15711081]
- Zieman, SJ.; Schulman, SP.; Fleg, J. Ischemic heart disease. In: Edwards, NM.; Maurer, MS.; Wellner, RB., editors. *Aging, heart disease, and its management: Facts and controversies: Contemporary Cardiology*. Totowa: Humana Press; 2003. p. 249-273.

Characteristics of those with hypertension taking a hypotensive medication and normotensive individuals not taking a hypotensive medication across covariates.

Table 1

Covariate	Normotensive		Hypertensive			
	n = 380 M(SD)	No Medication n = 168 M(SD)	ACE Inhibitor n = 115 M(SD)	ARB n = 47 M(SD)	Alpha Blocker n = 18 M(SD)	Beta Blocker n = 42 M(SD)
Age*	72.72 (5.91)	74.07 (5.62)	73.34 (5.79)	72.91 (5.42)	75.33 (5.60)	74.48 (6.79)
Education	14.19 (2.72)	13.68 (2.56)	13.71 (2.32)	14.19 (3.01)	14.22 (3.08)	13.90 (2.91)
Far Visual Acuity	72.77 (11.29)	70.81 (12.28)	69.63 (12.11)	69.73 (11.41)	71.82 (14.87)	70.72 (11.06)
Number of depressive symptoms**	6.92 (6.40)	8.39 (7.12)	8.47 (7.30)	8.53 (6.92)	4.17 (4.41)	6.52 (6.61)
Number of health conditions other than hypertension***	2.97 (2.18)	3.71 (2.27)	4.10 (2.24)	4.64 (2.52)	3.78 (2.16)	4.33 (2.20)

Note: Significant group differences as indicated by Analysis of Variance (ANOVA).

* p < .05,

** p < .01,

*** p < .001

Table 2

Cognitive performance (z-scores) across all conditions

Variable	Normotensive				Hypertensive			
	No Medication n = 168 M(SD)	ACE Inhibitor n = 115 M(SD)	ARB n = 47 M(SD)	Alpha Blocker n = 18 M(SD)	Beta Blocker n = 42 M(SD)			
Digit Span**	.140 (.967)	-.094 (.990)	-.290 (.930)	-.260 (.852)	-.181 (.956)			
Spatial Span	.112 (.935)	-.122 (.994)	-.005 (1.014)	-.064 (.605)	-.183 (1.032)			
HVLT	.127 (.907)	.068 (.972)	.039 (1.100)	-.283 (1.035)	-.297 (1.221)			
Trail Making Test A***†	-.205 (.527)	.085 (.748)	.013 (.739)	.048 (.613)	.215 (.723)			
Trail Making Test B***†	-.228 (.673)	.138 (.982)	-.053 (.796)	.149 (.885)	.226 (1.187)			
Digit Symbol Substitution***†	-.202 (.493)	.045 (.666)	.012 (.667)	.027 (.722)	.163 (.780)			
UFOV***†	-.201 (.838)	.136 (1.088)	.211 (.960)	-.170 (.788)	.190 (1.042)			
Letter Comparison**	.194 (.945)	-.113 (.986)	-.091 (1.156)	-.250 (.907)	-.366 (.989)			
Pattern Comparison**	.227 (.910)	-.150 (1.058)	-.027 (1.064)	-.050 (.825)	-.302 (.958)			
Road Sign Test***†	-.180 (.590)	.023 (.772)	.078 (.741)	-.167 (.435)	.104 (.896)			
Timed IADL†	-.077 (.514)	.039 (.760)	-.062 (.377)	.109 (.675)	.026 (.620)			
Motor Speed***†	-.240 (.687)	.113 (.872)	.009 (.741)	.627 (.627)	.250 (.992)			

Note: Significant group differences as indicated by Univariate ANCOVA.

* p < .05.

** p < .01.

*** p < .001

† lower scores reflect better performance