Cognitive Performance in Hypertensive and Normotensive Older Subjects

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Abstract—Longitudinal studies suggest that hypertension in midlife is associated with cognitive impairment in later life. Cross-sectional studies are difficult to interpret because blood pressure can change with onset of dementia and the inclusion of subjects on treatment and with hypertensive end-organ damage can make analysis difficult. We examined cognitive performance in hypertensive and normotensive subjects without dementia or stroke ≥70 years of age. Cognitive performance was determined with the use of a computerized assessment battery in 107 untreated hypertensives (55 women, age 76±4 years, blood pressure, 164±9/89±7; range, 138 to 179/68 to 99 mm Hg) and 116 normotensives (51 female, age 76±4 years, 131±10/74±7; 108 to 149/60 to 89 mm Hg). Older subjects with hypertension were significantly slower in all tests (reaction time, milliseconds; simple, 346±100 versus 318±56, P<0.05; memory scanning, 867±243 versus 789±159, P<0.01; immediate word recognition, 947±261 versus 886±192, P<0.05; and delayed word recognition, 937±230 versus 856±184, P<0.05; picture recognition, 952±184 versus 894±137, P<0.01; spatial memory, 1390±439 versus 1258±394, P<0.01; excepting choice reaction time, 510±75 versus 498±72, P=0.08). Accuracy was also impaired in tests of number vigilance, 99.2±2.5% versus 99.9±0.9, P<0.01; delayed word recognition, 83.5±16 versus 87.9±9.8, P<0.01; and spatial memory 64±32 versus 79±20, P<0.001. Hypertension in older subjects is associated with impaired cognition in a broad range of areas in the absence of clinically evident target organ damage. (Hypertension. 2000;36:1079-1082.)

Key Words: hypertension, arterial ■ blood pressure ■ aging ■ dementia

Cognitive impairment and dementia are becoming increasingly prevalent because of demographic changes. The prevalence of dementia doubles with each 5-year age rise, from 2.8% at 70 to 74 years to 38.6% at 90 to 95 years.1 The annual prevalence of dementia doubles with each 5-year age rise, from 2.8% at 70 to 74 years to 38.6% at 90 to 95 years.1 The annual incidence of dementia in the age group 85 to 88 years is 9%.2 Dementia incidence in a population >55 years of age was 10.7 per 1000 person-years, equating to a lifetime dementia risk for a 55-year-old woman of 0.33 and 0.16 for a man.3

The UK population >60 years of age is projected to increase by a third by the year 2026; the population with cognitive impairment is projected to double by 2026.4 In this context, population risk factors for the development of dementia that are potentially modifiable are important to identify. Cognitive impairment usually develops insidiously, eventually reaching a stage where it becomes clinically and functionally apparent. Studies of subjects with no or with minor cognitive impairment have shown that neuropsychological tests can predict who is likely to proceed to dementia.5

Hypertension is common in elderly Western populations, with a prevalence of 41% for men and 54% for women 75 years of age, defined by single blood pressure (BP) reading of >160 mm Hg systolic and/or >95 mm Hg diastolic or any treatment for hypertension.6 Epidemiological data from Birmingham7 suggested no association between BP and cognitive performance when measured concurrently; however, when data were reanalyzed the average BP over 20 years was inversely related to cognitive performance.8 Three further studies have shown a link between midlife or later-life hypertension and subsequent cognitive impairment.9–11 Reasons for discrepancies between cross-sectional and longitudinal studies may include the tendency for BP levels to change with the onset of dementia,10 the inclusion of individuals with established cerebrovascular disease in cross-sectional studies, and the effects of BP-lowering therapy on cognitive function. Except for one small study in 25 older patients with severe hypertension there are no data on cognitive function in older hypertensives where the effects of cerebrovascular disease have been excluded.12

The hypothesis of the present study was that cognitive performance in older adults without overt cerebrovascular disease would be impaired in line with increasing BP level. We determined cognitive performance in untreated older hypertensives and normotensives without cerebrovascular disease, target organ damage, or other vascular risk factors.

Methods

The study was performed in a community primary care population. Subjects were recruited from 10 local general practices in the

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Tyneside area. BP readings over the last 5 years, current drug therapy, and concomitant disease from all persons in the 70- to 89-year age group were recorded from general practitioner case records. Subjects who were not taking BP-lowering drugs, had no serious concomitant disease (dementia, malignancy, or advanced renal failure), and had BP readings recorded in the notes were contacted by letter and invited to attend the screening clinic; 1213 subjects attended. Hypertensive subjects were first recruited through screening of subjects with average recorded BP readings of >160 and/or 90 mm Hg. Normotensive subjects were subsequently recruited by screening of subjects with average BP readings of <150/90 mm Hg. BP was measured with a mercury sphygmomanometer 3 times on each of 3 occasions, each separated by 2 weeks. Baseline BP was defined as the mean of the second and third readings on the last of these 3 visits. Two cohorts of subjects were recruited: hypertensives with systolic BP 160 to 179 mm Hg and/or diastolic BP 90 to 99 mm Hg and normotensives with BP<150/90 mm Hg. Subjects were excluded if they were receiving any BP-lowering therapy, had atrial fibrillation, diabetes mellitus, previous stroke or transient ischemic attack (defined by clinical history or physical examination), cardiac bruits on auscultation, peripheral vascular disease (symptomatic claudication or absent foot pulses), angina or previous myocardial infarction (defined by clinical history or ECG changes), or dementia. Dementia was defined as mini mental state examination (MMSE) <24 and/or significant decline in cognitive function; this was assessed by interview with a close friend or relative and completion of Clinical Dementia Rating13 and IQ Code.14 Subjects taking psychotropic medication were also excluded because these drugs can interfere with cognitive function. Educational level was assessed by number of years at school and verbal IQ using number of errors in the New Adult Reading Test15 (NART). Subjects were screened for the presence of depressive disorder by the 30-point Geriatric Depression Scale16 (GDS). Studies were approved by the Newcastle Joint Ethics committee. All subjects gave informed, written consent.

**Cognitive Assessment**

Subjects were administered the Cognitive Drug Research Computerized Assessment Battery.17,18 The subject sits in front of a laptop computer, a series of words, pictures, and numbers appear on the screen and the subject responds by pressing “yes” or “no” on a button box in front of them. The battery comprises 8 tests and takes 20 minutes to administer.

Simple reaction time is a test of attention, alertness, and power of concentration. Choice reaction time is similar to simple reaction time with an element of stimulus discrimination and response. Immediate and delayed word recognition time test the ability to store and retrieve verbal information and discriminate novel from previously presented words. Picture recognition time tests the ability to store and retrieve pictorial information and discriminate novel from previously presented pictures. Memory scanning reaction time tests the ability to store and retrieve visual spatial information. Memory scanning tests the ability to store information in the working memory and rapidly retrieve it, testing subvocal rehearsal of digit sequences.

The computerized battery was administered once as a training session before baseline. Preliminary studies with a subgroup established that 1 training session was sufficient to familiarize the subjects with the test system.

**Statistical Analysis**

Data were analyzed with SPSS for Windows. Statistical significance was set at the 5% level. Means were analyzed by means of the independent samples t test.

**Results**

One hundred seven untreated hypertensives (164±9/89±7; range, 138 to 179/68–99 mm Hg, 55 women) and 116 normotensives (131±10/74±7; 108 to 149/60–89 mm Hg, 50 women) were studied. Mean age (76±4 years), years in education (10±2), and MMSE score (29±1) were identical in both groups. There was no significant difference in hypertensive and normotensive group NART scores (19.3±9.2 versus 17.5±8.6) or GDS scores (5.4±4.6 versus 5.0±4.5). Ten subjects in each group were taking aspirin. Results of the cognitive assessment battery in hypertensive and normotensive groups are shown in the Table. The hypertensive group was significantly slower in all tests except for choice reaction time, in which the slower response was of borderline significance. Accuracy of response in hypertensive subjects was also impaired for number vigilance, delayed word recognition, and spatial memory.

**Discussion**

We have shown by using a cognitive assessment instrument that has been well validated in the elderly that older subjects with hypertension but without clinical evidence of vascular disease have impaired cognition in a broad range of tests of attention and short- and long-term memory. Hypertensives were on average 10% slower in psychomotor tests compared with normotensive peers. The decrement seen in the hypertensive subjects is one-third to one-half that seen in mild dementia. A study using the CDR battery in subjects with mild Alzheimers dementia (MMSE 24) and healthy age-matched control subjects without dementia (MMSE 29) found the dementia group to be slower by 13% to 44% in the tests.19

These differences may not be sufficient to interfere with activities of daily living and would not be recognized in routine clinical practice because of wide interindividual variability. However, many studies have observed that premorbid cognitive function levels are associated with increased risk of developing dementia.5,20,21 The public health implications of relatively small individual declines in cogni-
tion are large when applied to a population. The presence of vascular risk factors in some population subgroups was associated with a left shift of the normal distribution of MMSE scores and a large increase in numbers of individuals falling below the cutoff score for probable dementia.22

The majority of studies examining the effect of BP on cognition have looked at BP levels very much higher than those in the present study. We have found important impairments in cognitive function in a group of older hypertensives with only moderately increased BP. This has implications for the large numbers of elderly people with only minimally raised BP. Results from this study agree with those from a previous smaller study12 of more severe hypertensives (mean age, 70.6 years; mean BP, 192/112) and normotensives (mean age, 70.4 years; mean BP, 143/80). The hypertensives were rigorously screened to exclude those with end-organ damage, although the majority of hypertensives had been on treatment and were tested off treatment. This study found the hypertensives to be significantly slower in tests of attention and psychomotor speed. The present study confirms these observations and extends the findings to older subjects with lesser degrees of BP elevation. Interpretation of cross-sectional studies is difficult for a number of reasons, including use of wide age ranges,23–25 use of tests not validated in the elderly, use of combinations of treated and untreated subjects,25 subjects with likely end organ damage,26 inclusion of subjects with probable dementia,27 and too few BP readings to adequately define BP status and level.28,29 However, repeated BP measurements in this study clearly characterize participants BP status may have had the disadvantage of “labeling” subjects, which may have led subjects who were aware that they were hypertensive to perform less well. However, it is also possible that low levels of anxiety, generated by “labeling” of subjects as hypertensive, may have enhanced some aspects of cognitive performance.

The differences seen in our study are likely to be due to a direct effect of hypertension. The groups are well matched for other factors known to influence cognitive function: age, educational level, depressive disorder, and psychotropic medication. There are a number of possible mechanisms through which hypertension might directly impair cognitive function. Ischemic stroke increases the risk of dementia.30–32 The hypertensive subjects in our study had no clinical evidence of cerebrovascular disease or other target organ damage from hypertension. However, an increased prevalence of asymptomatic cerebrovascular disease may have been present in the hypertensive subjects. Multiple small infarcts can lead to dementia, depending on volume of brain affected,33,34 location of infarcts, and bilateralality. White matter lesions that consist of areas of demyelination and narrowing of small arteriolar lumen size have been associated both with hypertension and with cognitive dysfunction. The presence of brain MRI white matter lesions is associated with impaired cognitive functioning in subjects with and without dementia.35,36

Other possible mechanisms are changes in cerebral auto-regulation37 and cerebral blood flow38 associated with hypertension. Kalra et al39 reported improvements in tests of attention and psychomotor speed when 25 elderly hypertensive subjects were treated with BP-lowering therapy (n = 20) or placebo (n = 5). These observations require confirmation, but such reversibility would suggest that psychomotor impairment is a direct consequence of hypertension, most likely mediated through effects on cerebral blood flow or metabolism.

Genotypic influences that contribute to hypertension could influence cognition through common or separate mechanisms. A potential genetic link factor between hypertension and cognitive impairment is the apolipoprotein E allele, which has been linked to vascular risk factors,40 coronary artery disease,41,42 and stroke,43 as well as Alzheimer’s dementia.44,45 In postmortem studies,46,47 an increased e4 allele frequency has been reported in subjects with hypertension or critical coronary artery disease and an increased number of senile plaques and neurofibrillary tangles in the brains of apoE4-positive hypertensives who were not demented. Further work is needed to explore the link between apoE4 and hypertension and cognitive impairment in older people.

Our observations do not necessarily imply that treatment of hypertension will reduce cognitive decline. However, the SystEur Vascular Dementia project48 reported treatment of hypertension in the elderly with the calcium channel blocker nitrendipine reduced incidence of dementia by 50%. A recent longitudinal observational study also suggests that treatment of hypertension in older individuals may reduce cognitive decline.49 Hypertension was associated with cognitive decline during 4 years of follow-up, with the highest risk in untreated patients. If treating hypertension reduces the rate of cognitive decline, the benefits of treating hypertension would extend beyond the prevention of stroke and myocardial infarction to primary prevention of dementia. The present findings support undertaking further studies to elucidate the mechanisms through which hypertension is associated with cognitive impairment and intervention studies to determine whether treatment of hypertension prevents dementia.

Acknowledgments

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