The Relationship between Changes in Normal-Range Systolic Blood Pressure and Cognitive Function in Middle-Aged Healthy Women

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Little is known about the effect of normal-range blood pressure (BP) on cognitive function. In previous studies investigating the relationship between BP and cognitive function in elderly subjects, underlying cerebrovascular damage has complicated the interpretation of results. To reveal the relationship between BP levels that were within an absolutely normal range and cognitive function, we examined cognitive function in normotensive, healthy middle-aged women. BP levels were measured on three separate occasions at 1-month intervals, and the subjects exhibiting normotension (<140/90 mmHg) throughout the evaluation period were recruited as normotensive subjects. Cognitive function was assessed using subtests of the Wechsler Adult Intelligence Scale—Revised. The study demonstrated that, among the subtests examined, the scores on the Digit Symbol Test, an index of psychomotor performance, had a significant correlation with normotensive-range systolic blood pressure (SBP) (r = -0.51, p < 0.05); this relation was negative—that is, higher but still normal-range SBP levels were associated with impaired Digit Symbol Test scores. In addition, the relationship adjusted by age and educational level was also significant (partial correlation = -0.56, p < 0.05). In contrast, diastolic BP was not related to the Digit Symbol Test (r = -0.33, p = 0.13). Furthermore, the Digit Symbol Test was not influenced by blood glucose or serum cholesterol levels. These findings suggested that, even within the normotensive range, lower levels of SBP might be protective against impairment of psychomotor speed in middle-aged women. (Hypertens Res 2002; 25: 565–569)

Key Words: systolic blood pressure, cognitive function, Digit Symbol Test, psychomotor speed

Introduction

Impairment of cognitive function in the elderly is an area of great concern across the world. Cognitive dysfunction impairs the abilities of daily life and reduces participation in social activities through deterioration in memory, attention, perception, mental flexibility, and psychomotor performance. More seriously, cognitive impairment can progress to dementia (1). In addition, for all of the above reasons, subjects with cognitive dysfunction require substantial assistance from their families and societies in order to support their daily lives.

Hypertension is well related to cognitive deterioration. In addition, a recent large clinical trial, the Syst-Eur trial, has demonstrated that blood pressure (BP) reduction in systolic hypertension is associated with an approximately 50% decrease in dementia (2). Unfortunately, however, how far BP should be lowered to achieve the greatest benefits in terms of protection of cognition remains to be answered.

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Furthermore, the relationship between changes in normal-range BP and cognitive function, particularly the implications of lower BP, remains to be clarified. In fact, there have been few studies directly exploring the effect of low BP on cognitive function. Guo et al. (3) have reported that low-level BP is related to an impairment of cognition. On the other hand, J-curve (4) or U-shaped (5) relationships between BP values and performance on cognitive tests have also been reported. However, the subjects in these studies were elderly, mostly over 75 years old, and included patients who had suffered from hypertension for a long period. In such subjects, BP reduction is likely to cause cerebrovascular hypoperfusion through a resetting of hemodynamic autoregulation. Moreover, it has also been reported that cerebrovascular diseases or dementia underlying cognitive impairment lowers BP per se, thereby producing a further deterioration of cognitive function (6, 7). Thus the elderly cohorts used in previous studies have tended to complicate the interpretation of the relationship between BP and cognitive function. Hence, to explore the possible effect of lower levels of BP on cognitive function, younger and healthier subjects who are less likely to have suffered from cerebrovascular damage should be analyzed. Accordingly, we here used a cohort of normotensive, middle-aged women to explore the effects of lower levels of BP on cognitive function.

Subjects and Methods

Subjects

Among post-menopausal women who visited our Health Service Center for medical check-ups, 26 women aged 56 to 60 years old were recruited randomly for participation in the present study. All the subjects were well informed of the objective and outlines of the tests and gave their informed consent to participate in this project. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured 3 times at 1-month intervals by a well-trained registered nurse. At each visit for BP determination, BP was measured 3 times at 5-min intervals in the morning with subjects in a seated position after 30-min of relaxation in a quiet room, and then was measured. The criteria for normotension were <140 mmHg for SBP and <90 mmHg for DBP according to the classification recommended by 1999 WHO/ISH (8). Twenty-two subjects were diagnosed as normotensive because their BP values were all within the normal range throughout the evaluation period. Four subjects were hypertensive, including 1 subject who was taking anti-hypertensive drugs. These 4 cases were excluded, and the remaining 22 subjects were analyzed in this study. None of the subjects had a history of stroke or any signs/symptoms suggestive of established dementia or disorders of the central nervous system. None of the subjects were taking medicines that would affect cognitive function.

Physical Measurements

All measurements of SBP and DBP of each subject were averaged respectively, and the values were used for the following analyses. At the last visit for BP evaluation, heart rate (HR), body weight, and height were also measured using standard electrical devices. Body mass index (BMI) was defined as body weight (kg) / (height (m))^2. In addition, blood samples were obtained to determine serum concentrations of total cholesterol (TC) and fasting blood glucose (FBS).

Psychometric Assessments

After measuring physical characteristics, psychometric tests, including Wechsler Adult Intelligence Scale-Revised (WAIS-R) subtests, were administered by a designated specialist for psychological examination. The examiner was blinded to all patient characteristics. Standardized procedures from published manuals were used in the test administration and evaluation. Cognitive function was measured using WAIS-R subtests (9), which are widely used instruments for evaluating intelligence in adults. Because it takes so long time to perform a full set of WAIS-R subtests, eight subtests were selected and administered in the present study: 1) Information, 2) Digit Span, 3) Similarities, 4) Picture Completion, 5) Picture Arrangement, 6) Block Design, 7) Object Assembly, and 8) Digit Symbol. The Digit Symbol Test largely reflects psychomotor speed and is independent of influences from the other factors (10). Scores for each subtest were expressed as the percentage of correct responses. The Yatabe-Guilford (Y-G) test (11), which is a self-reported, multiple-choice questionnaire, was used to evaluate the character traits of the subjects.

Educational Level

Educational level was expressed as the total length of education: i.e., 6 years for elementary school, 3 years for junior high school, 3 years for senior high school, 2 years for technical college, 2 years for junior college, 4 years for university, and 2 years for graduate school.

Statistical Analysis

Statistical analyses were performed using STATISTICA software (StatSoft, Tulsa, USA) on a computer running the Windows operating system. To test the possible relationship between cognitive tests and BP, both simple correlations and partial correlations controlling for the effects of other variables were examined. Stepwise multiple regression analysis was also performed to find the most important predictor variables for cognitive test scores.
Results

Basal Characteristics of the Subjects

The basal characteristics of the subjects are shown in Table 1. The range of SBP was 100–138 mmHg, and that of DBP was 50–88 mmHg. SBP and DBP were not related to age, BMI or HR. There was no correlation between BP level and either TC or FBS. The values of demographic characteristics exhibited a normal distribution pattern when assessed by the Shapiro-Wilk’s W test (data not shown). Cognitive test scores of the subjects are shown in Table 2. The mean score of the WAIS-R subtests, excluding the Digit Symbol Test, was within the normal range for Japanese aged 55 to 64 years. The average score of the Digit Symbol Test (67.4) was slightly higher than the normal range for Japanese of this age group (30.1–61.3).

The values of risk factors shown in Table 1 and the score of cognitive tests were mostly within the normal range, and there was no polarization among these values. These data indicated that the group employed in the present study was a non-deviated, representative cohort of healthy middle-aged Japanese women.

Association of Blood Pressure with Cognitive Functions

The results clearly demonstrated that SBP was related to the Digit Symbol Test (r = -0.51, p < 0.05) (Fig. 1), which principally reflects psychomotor speed. In contrast, DBP was not related to the Digit Symbol Test (r = -0.33, p = 0.13) (data not shown).

Cognitive test scores are known to be influenced by age and educational attainment (J2). In particular, age could cause a spurious negative correlation between the SBP and the Digit Symbol Test due to its positive correlation with the SBP and negative correlation with the Digit Symbol Test. To examine this possibility, we computed a partial correlation between the SBP and the Digit Symbol Test controlling for the effects of age, and obtained the value of -0.55 (p < 0.05), which is even higher than the simple correlation reported above.

By also controlling for educational level, we could focus...
Table 4. Important Predictors of the Digit Symbol Test Based on Multiple Stepwise Regression Analysis

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<tr>
<th>Risk factors</th>
<th>β</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age</td>
<td>-0.52</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SBP</td>
<td>-0.39</td>
<td>&lt;0.05</td>
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Multiple correlation coefficient: $r^2 = 0.48$, $F = 5.70$ ($p < 0.05$). The dependent variable is the score on the Digit Symbol Test. Independent variables included in the multiple stepwise regression analysis are age, education, SBP, heart rate, body mass index, glucose, and total cholesterol.

Discussion

In the present study, we demonstrated a negative correlation between SBP within normotensive range and the Digit Symbol Test for assessing psychomotor speed ability. In some previous studies, a broad range of BP levels from normotension to severe hypertension was analyzed and they found an inverse linear correlation between BP level and score of cognitive tests (15, 16). These results are believed to reflect the effects of severe hypertension on cognitive function. That is, while these studies highlighted the influence of high BP per se, they did not isolate the role of normal-range BP. In this sense, we revealed the close association between the BP within normal range and cognitive function for the first time.

We examined cognitive function in apparently normal subjects. For this reason, any changes in cognitive function were likely to be slight. This prompted us to use the WAIS-R test to assess the decline in cognitive function, since this test is more sensitive than the standard diagnostic tools of dementia, i.e., the Mini-Mental State Examination and revised version of Hasegawa’s Dementia Scale. In this study, eight WAIS-R subtests were administered, with each constructed to assess a different aspect of cognitive function. Among the eight WAIS-R subtests, only the Digit Symbol Test for assessing psychomotor speed ability was correlated with SBP values. Several previous studies have reported that the effect of hypertension is the most consistent for psychomotor speed and mental status measure (12). On the other hand, crystallized domain, i.e., information and similarities, is the most stable and resistant to BP effects (12, 16). A decline in Digit Symbol Test values is also known to be associated with parietotemporal perfusion defects (17). Parietotemporal perfusion is regulated by branches of the internal carotid artery, and is subject to arterial injury following increases in BP. The correlation between Digit Symbol Test values and SBP within normal range may be mediated by the liability of blood perfusion in the particular blood vessels. Another possibility is that only the most powerful association is detected because of the narrow range of BP.

We demonstrated that normotensive SBP, but not DBP, is associated with reduced cognitive function. Some of the longitudinal, prospective studies have emphasized the role of higher SBP, rather than DBP, in cognitive decline in the elderly (18–20). In consideration of these data, we cannot overestimate the importance of midlife SBP values on eventual cognitive impairment. It was beyond the scope of the present study to clarify the mechanisms underlying the relationship between SBP and cognitive dysfunction. However, Swan et al. (21) have demonstrated that the long-term effects of SBP in midlife on deterioration of cognitive function in late-life are mediated by cerebrovascular lesions. In fact, two different groups have revealed that not only high SBP, but also moderate increase in SBP within normal range, behaves as an independent risk factor for silent lacunar infarcts (22, 23). All things considered, it seems probable that a moderate increase in SBP in midlife already exerts a direct effect on cerebral vascular vessels and produces brain dysfunction.

We were unable to confirm previous reports of an association between lower BP and cognitive decline (3–5). Since our healthy, normotensive subjects were presumably free from cerebrovascular damage, the J-shape-like phenomenon was not found in our study.

Metabolic disturbances, especially in lipid and glucose metabolisms, are considered to be associated with cognitive function through cerebrovascular lesions. In studies from other laboratories, hyperinsulinemia, diabetes mellitus, or hypercholesterolemia have been reported to contribute to impaired cognitive function (24, 25). In this study, however, we demonstrated that mild abnormalities in levels of FBS or serum TC did not influence cognitive function.

One limitation of the present study is the small sample size. However, it should be noted that a statistically significant correlation was obtained between BP and cognitive function. We were unable to confirm previous reports of an association between lower BP and cognitive decline (3–5). Since our healthy, normotensive subjects were presumably free from cerebrovascular damage, the J-shape-like phenomenon was not found in our study.

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functions regardless of the insufficient statistical power due to the small sample size, and regardless of the limited range of BP, which tends to decrease the size of correlation.

In conclusion, a moderate increase in SBP within normotensive range appears to be related to cognitive deterioration. To sustain the cognitive function, a lower SBP is ideal in normotensive, middle-aged women. In addition, a decline in Digit Symbol Test values has been reported to be a marker in normotensive, middle-aged women. In addition, a decline in normotensive range appears to be related to cognitive deterioration.

Regardless of the small sample size, and regardless of the limited range of BP, which tends to decrease the size of correlation, our present findings. A prospective study will be needed as a next step to confirm our present findings.

References