Original Article

The Effects of Short-Term Blood Pressure Variability and Nighttime Blood Pressure Levels on Cognitive Function

Akiko KANEMARU, Kazutomi KANEMARU*, and Iwao KUWAJIMA

We investigated the relationship between 24-h blood pressure (BP) and cognitive function. We performed the Hasegawa Dementia Scale Revised (HDSR), the Mini-Mental State Examination (MMSE), and the Raven's Coloured Progressive Matrices Test (RCPM) in 88 subjects (71 ± 9 years) with no history of stroke. Ambulatory BP was non-invasively measured using a TM2421 for 24 h in all patients. Whereas 90% of the scores converged into a narrow range between 25 and 30 points in the HDSR and the MMSE tests, the RCPM score was widely distributed, ranging from 9 to 36 points. The subjects were therefore divided into three groups of ≥ 25 , 26–30, and 31–36 according to their RCPM scores. Subjects with lower scores were significantly associated with increased short-term BP variability during the daytime ($p < 0.05$) and had a tendency toward higher nighttime SBP ($p = 0.05$) compared with those with higher scores. Increased short-term variability of daytime BP and high nighttime systolic BP were associated with cognitive impairment as assessed by the RCPM. The RCPM, which can assess the capacity for judgment through visual information processing, may detect earlier stages of cognitive impairment related to high BP. To prevent a deterioration of cognitive function, strict control of nighttime BP and suppression of short-term BP variability are thus necessary. (*Hypertens Res* 2001; 24: 19–24)

Key Words: blood pressure, variability, nighttime, cognitive function

Introduction

Many epidemiologic studies have shown that hypertension is related to cognitive function (1, 2). The Honolulu-Asia Aging Study showed that systolic BP during middle age is a significant predictor of cognitive impairment in later life and that early control of systolic BP levels may reduce the risk of cognitive impairment in old age (3). Although increased BP may increase the risk of dementia involving small-vessel disease and white matter lesions, it remains to be clarified whether the decline in BP seen in patients with dementia onset is a consequence or a cause of the brain disease (4). Prince *et al.* (5) have found no significant relationship between BP reductions achieved with

diuretics or β blockers and subsequent cognitive function in moderately elderly hypertensive patients. However, a recent randomized double-blind clinical trial clearly demonstrated that reduced blood pressure treated with a long-acting calcium channel blocker is associated with a lower incidence of dementia in elderly hypertensive patients (6).

Since the development of the ambulatory blood pressure monitoring (ABPM) device, much information that had not previously been obtainable from office blood pressure measurements became available (7–9). Actually, the accumulating findings indicate that the ambulatory blood pressure is superior to office BP for predicting future cardiovascular events (10). In addition, the clinical implications of nighttime BP and daytime BP variability have received much attention in terms of silent cerebro-

From the Departments of Cardiology and *Neurology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan.

Address for Reprints: Akiko Kanemaru, M.D., Department of Cardiology, Tokyo Metropolitan Geriatric Hospital, 35-2 Sakae-cho, Itabashi-ku, Tokyo 173-0015, Japan.

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Table 1. Characteristics of Subjects and 24-Hour Blood Pressure

Sex (M : F)	35 : 53
Age (y.o.)	71 ± 9
Education (years)	10.0 ± 2.9
Antihypertensive treatment (Yes : NO)	28 : 60
Office blood pressure (mmHg)	161 ± 23 / 85 ± 13
24-h blood pressure	
Total average (mmHg)	142 ± 15 / 80 ± 10
Daytime average (mmHg)	144 ± 15 / 81 ± 10
Mean SD of daytime BP	17.5 ± 4.5 / 10.8 ± 2.4
Nighttime average (mmHg)	133 ± 18 / 73 ± 11
Mean SD of nighttime BP	13.2 ± 4.3 / 8.4 ± 2.3

vascular damage (11).

In the present study, we examined whether the levels or variability in 24-h blood pressure can have some effect on cognitive function.

Subjects and Methods

Subjects

Of the 238 consecutive cases who visited the hypertension clinic of the Tokyo Metropolitan Geriatric Hospital for the evaluation of hypertension, 88 cases without history of cerebrovascular disease, disturbance of the autonomic nervous system, diabetes mellitus, or apparent visual disturbance were involved in the present study. Their mean age was 71 ± 9 years, ranging from 37 to 90 years old. Twenty-eight cases were on antihypertensive medication (calcium antagonists, angiotensin-converting enzyme inhibitors, $\alpha\beta$ blockers, or diuretics). Informed consent was obtained from all subjects who participated in the study.

Blood Pressure Measurements

Office blood pressure was measured in the sitting position by physicians using a sphygmomanometer on a couple of occasions. The 24-h ambulatory blood pressure monitorings were performed non-invasively using a TM2421 (A&D Ltd., Tokyo) by the oscillometric method every 15 min between 6:00 and 21:00 and every 30 min between 21:00 and 6:00. Based on the diary the patient recorded, the 24-h blood pressures were separated into daytime and nighttime. Short-term blood pressure variability was expressed as SD of daytime BP. Subjects who complained of sleep disturbances during ambulatory BP monitoring were excluded from the present study.

Cognitive and Neuropsychological Assessment

We performed three tests to assess cognitive and neuro-

behavioral function: the Hasegawa Dementia Scale Revised (HDSR) (12), the Mini-Mental State Examination (MMSE) (13), and the Raven's Coloured Progressive Matrices Test (RCPM) (14). The HDSR, a Japanese screening test for dementia, consists primarily of items designed to assess orientation, verbal memory, calculational ability, and verbal fluency, with scores ranging from 0 to 30. The MMSE has items indicative of constructional ability compared with the HDSR. Whereas the HDSR and MMSE tests were performed by verbal communication, the RCPM test assesses the capability of imaginary identification of similarity and symmetry in addition to the analogical and conceptual thinking capacity without requiring verbal-processing skills. All three neuropsychological tests were performed by a skilled technician within 2 weeks of the time of the 24-h BP monitoring.

Statistical Analysis

All values are shown as mean ± SD. First, to evaluate the relationship between BP and cognitive function as obtained from each test, we performed a simple regression analysis between the score of each test and various factors that might affect cognitive function, including age, the 24-h BP, the daytime BP, the nighttime BP, and the standard deviations (SD) of each BP. Next, we performed a one-way analysis of variance (ANOVA) or chi-square analysis (χ^2) to compare the three groups divided by the RCPM score (≤ 25 , 26-30, 31-36), which is explained in Results. If the findings showed an inhomogeneity of variances, we used the Kruskal-Wallis one-way ANOVA.

Results

The office BP was 161 ± 23 for systolic pressure and 85 ± 13 mmHg for diastolic, and the 24-h blood pressure was 142 ± 15/80 ± 10 mmHg. The office BP was significantly higher than the 24-h BP. The daytime and nighttime systolic BPs were 144 ± 15 and 133 ± 18 mmHg, respectively. The daytime and nighttime diastolic BP were 81 ± 10 and 73 ± 11 mmHg, respectively (Table 1). Both systolic and diastolic BP were higher during the day than the night (both $p < 0.001$, t -test).

Although the HDSR and MMSE scores ranged from 17 to 30 and from 20 to 30, respectively, approximately 90% of the scores obtained from subjects converged into a narrow range between 25 and 30 points. In contrast, the score of the RCPM was widely distributed, ranging from 9 to 36 points (Fig. 1). We therefore divided the cases into the following three groups according to the RCPM score.

≤ 25 : severely affected (group 1, $n=11$)

26-30: moderately affected (group 2, $n=34$)

31-36: mildly affected/almost normal (group 3, $n=43$)

A comparison of age and BP parameters among these

Table 2. Office and Ambulatory Blood Pressure by Levels of Raven's Coloured Progressive Matrices Test (RCPM) Scores

RCPM score		Severely affected group 1, ≤ 25	Moderately affected group 2, 26-30	Mildly affected/Normal group 3, 31-36	
<i>n</i>		11	34	43	
Age		76 $\pm$ 8	70 $\pm$ 8	70 $\pm$ 9	n.s.
Education		9.2 $\pm$ 3.1	10.0 $\pm$ 2.0	10.2 $\pm$ 3.4	n.s.
Office SBP		161 $\pm$ 17	159 $\pm$ 20	162 $\pm$ 27	n.s.
DBP		87 $\pm$ 10	84 $\pm$ 11	86 $\pm$ 15	n.s.
Ambulatory BP					
24 h SBP		148 $\pm$ 18	142 $\pm$ 12	140 $\pm$ 16	n.s.
DBP		80 $\pm$ 10	80 $\pm$ 8	80 $\pm$ 11	n.s.
Daytime SBP		148 $\pm$ 20	144 $\pm$ 12	142 $\pm$ 16	n.s.
SD of SBP		18.5 $\pm$ 3.8	18.9 $\pm$ 5.5	16.0 $\pm$ 3.2	$p < 0.05$
DBP		80 $\pm$ 11	82 $\pm$ 8	81 $\pm$ 11	n.s.
SD of DBP		10.8 $\pm$ 2.4	11.5 $\pm$ 2.8	10.2 $\pm$ 1.9	$p < 0.05$
Nighttime SBP		145 $\pm$ 22	133 $\pm$ 16	130 $\pm$ 17	$p = 0.05$
SD of SBP		15.2 $\pm$ 6.3	13.3 $\pm$ 4.0	12.7 $\pm$ 3.8	n.s.
DBP		78 $\pm$ 10	73 $\pm$ 9	72 $\pm$ 11	n.s.
SD of DBP		8.6 $\pm$ 2.3	8.6 $\pm$ 2.2	8.3 $\pm$ 2.4	n.s.
Difference of day-night SBP		3.1 $\pm$ 19.5	11.8 $\pm$ 14.5	12.1 $\pm$ 10.8	n.s.
DBP		2.4 $\pm$ 8.3	8.7 $\pm$ 7.3	9.3 $\pm$ 6.7	$p < 0.05$

n.s., not significant; SBP, systolic blood pressure; DBP, diastolic blood pressure. Values are mean $\pm$ SD.

Fig. 1. Distribution of three different neuropsychological test scores in 88 subjects. Hasegawa Dementia Scale Revised (HDSR), Mini-Mental State Examination (MMSE), and Raven's Coloured Progressive Matrices Test (RCPM).

three groups is shown in Table 2. The differences in ages and the mean educational periods among the three groups were not significant.

The office and 24-h BPs showed no significant differences among the three groups in terms of systolic and diastolic BP. However, there were significant differences among the three groups in the SD for the daytime systolic BP ($p < 0.05$) and diastolic BP ($p < 0.05$), the nighttime

systolic BP ($p = 0.05$), and the day-night difference of the diastolic BP ($p < 0.05$) (Figs. 2-4). The difference in the magnitude of the day-night systolic BP dip was not significant. In summary, the most seriously disturbed group in terms of cognitive function assessed by the RCPM score had a significantly higher nighttime systolic BP in addition to greater short-term variability of the daytime BP.

The multiple regression analysis, in which the RCPM

Fig. 2. Daytime systolic blood pressure (SBP) and short-term variability of daytime SBP estimated by SD of SBP in three groups divided according to Raven's Coloured Progressive Matrices Test (RCPM) scores.

Fig. 3. Nighttime systolic blood pressure (SBP) in three groups divided according to Raven's Coloured Progressive Matrices Test (RCPM) scores.

score was used as the dependent variable and age, educational periods, and BP parameters (the variability of the daytime BP or the nighttime systolic BP) were used as the independent variables, showed that no variables were significant.

Discussion

We have demonstrated in the present study that increased BP variability and high nighttime systolic BP are related to cognitive impairment. Although we do not show cerebral CT and MRI findings herein, we did find that asymptomatic lacunar infarction and white matter lesions were associated with cognitive decline (15, 16).

A relation between increased daytime BP variability and target-organ damage has been reported previously

(17-19). Increased BP variability, estimated as the SD, is associated with hypertensive cardiovascular complications such as left ventricular hypertrophy (17, 18), and Binswanger's subcortical encephalopathy (19). In Binswanger-type dementia, widespread white matter lesions are observed on MRI. Recently, PET studies have shown that white matter lesions are closely related to a reduction in cerebral blood flow (20). Intermittent reductions in cerebral blood flow due to BP oscillations may contribute to the proliferation of white matter lesions and cognitive impairment.

In the present study, a high nighttime systolic BP was also related to cognitive impairment. Several studies have shown that reduced levels of nighttime BP fall (non-dipper) and high nighttime systolic BP are related to hypertensive target-organ damage, including lacunar infarction and white matter lesions in the brain (7, 11, 19, 21, 22). More precisely, the present study has shown that cognitive impairment is related to nighttime systolic BP levels but not to the magnitude of the nocturnal systolic BP dip, suggesting that the absolute values of nighttime systolic BP are more important for the development of lacunar infarction and white matter lesions. These findings are consistent with a recent longitudinal study by Staessen *et al.*, who demonstrated that nighttime systolic BP levels are related to cardiovascular risk (Syst-Eur Trial) (10). Van Boxtel *et al.* (23) have reported that non-dipping in 24-h ABPM is not related to cognitive impairment. In that study, although the subjects showed a non-dipping pattern, the absolute values of nighttime systolic BP were relatively low (129 ± 18).

Irie *et al.* (24), however, have reported that although BP was not evaluated by ABPM in their study, the J-curve phenomenon presents itself in the recurrence of stroke, and Nakamura *et al.* (25) have reported that nocturnal BP fall is related to the recurrence of stroke and

Fig. 4. The differences in daytime and nighttime blood pressures in three groups divided according to Raven's Coloured Progressive Matrices Test (RCPM) scores. SBP, systolic blood pressure; DBP, diastolic blood pressure.

the development of silent ischemic lesions. However, in the present study, cognitive impairment was not related to excessive nocturnal BP fall. Sustained elevated levels of BP, especially at night, may thus contribute to ischemic cerebral damage and cognitive impairment.

Finally, it should be noted that we detected cognitive impairment using the RCPM. RCPM is a non-verbal cognitive function test that can assess the capacity for judgment through uncomplicated visual information processing (14). This test may be useful in detecting the early stages of cognitive impairment related to high BP.

In conclusion, increased BP variability and high nighttime systolic BP appear to be related to cognitive impairment. To prevent the deterioration of cognitive function, suppression of short-term BP variability and strict control of the level of nighttime BP are needed.

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