Hypertension Is Related to Cognitive Impairment
A 20-Year Follow-up of 999 Men

Lena Kilander, Håkan Nyman, Merike Boberg, Lennart Hansson, Hans Lithell

Abstract—Recent findings of a linkage between high blood pressure (BP) and later development of dementia have given new prospects on cerebral target-organ damage in hypertension and have added substance to the concept of “preventable senility.” The aim of this study was to analyze the impact of hypertension, circadian BP profile, and disturbed glucose metabolism on cognitive function. The study population consisted of 999 seventy-year-old men from a population-based cohort study in Uppsala, Sweden, followed with respect to cardiovascular risk factors since the age of 50 years. At the age of 70, 24-hour ambulatory BP was monitored together with measurements of insulin sensitivity, glucose tolerance, serum lipids, and lipoproteins. Cognitive function was assessed by the Mini-Mental State Examination and the Trail-Making Test. High diastolic BP at baseline predicted later impaired cognitive performance, even after excluding men with a previous stroke (n=70). Cross-sectional measurements at age 70 showed that high 24-hour BP, nondipping, insulin resistance, and diabetes all were related to low cognitive function. The relationships between hypertension and cognitive impairment were strongest in untreated men. These data from a general population of healthy elderly men indicate that hypertension and associated metabolic disturbances might be susceptibility factors for cognitive disorders. The findings add support to possibilities of intervention in early stages in cognitive decline, i.e., before manifest dementia. (Hypertension. 1998;31:780-786.)

Key Words: cognition ■ blood pressure monitoring, ambulatory ■ diabetes ■ insulin resistance

The question of whether some degree of cognitive deterioration is an inevitable part of aging or should be considered as a pathological prestage of dementia is currently debated. This is a field in need of research1 because further decline in cognition might be preventable in the early stages of “cognitive impairment nondementia.” Vascular dementia is a common form of dementia; in the oldest elderly patients it is as frequent as Alzheimer’s disease.2 Recently, a 15-year follow-up study showed that high BP predicted dementia in the oldest elderly patients, irrespective of subtype.1 Little is known about how cognitive function is affected by vascular risk factors in the general population. The aim of the present study was to analyze the associations between BP, diurnal BP variation, disturbances in glucose and lipid metabolism, and cognition. We examined cognitive functions in a population-based cohort of 70-year-old men in which longitudinal measurements of vascular risk factors were available.

Methods
The study population consisted of 999 men. They were participants in a health survey focusing on cardiovascular risk factors that was started in the beginning of the 1970s in Uppsala, Sweden. The original cohort was defined as all men born in 1920 to 1924, who resided in the municipality of Uppsala in 1970 to 1973 (n=2841). A total of 2322 (81.7%) men participated in the baseline examination at 50 years of age.1 As a result of this first survey, medical and/or dietary treatment were offered to 126 men with hypertension, to 363 men with hyperlipidemia, and to 112 men with impaired glucose tolerance.1 A new examination was carried out when they were 60 years of age, in which 1860 of the 2130 remaining men from the original study cohort participated. In January of 1991, 422 subjects from the 50-year study had died. Of the 1900 men still alive, those who lived in Uppsala county (n=1681) were invited to a more extensive health examination, in which 1221 men (72.6%) took part. These men were also invited to a psychometric testing, in which 999 men (82%) took part. Their mean age was 72.4 years (range, 69 to 75 years).

Vascular Risk Factors
From the baseline examination at age 50 years, data for the following measurements were collected: office SBP and DBP measured in the supine position after 10 minutes rest with a mercury manometer to the nearest 0 or 5 mm Hg; BMI calculated as weight (in kilograms) divided by the height squared (in meters); and fasting concentrations of blood glucose, serum insulin (n=815), HDL cholesterol (n=801), and serum triglycerides. The study protocol has previously been described in detail.3 Values of serum lipids and lipoproteins were later standardized to correspond to the methods used for the 70-year survey. From the 60-year survey, data on office BP, measured as described above, and antihypertensive treatment from a questionnaire were collected. At the 70-year survey, the investigations included office SBP and DBP in the supine position, measured with a sphygmomanometer to the nearest 2 mm Hg (mean of two measurements), calculation of BMI, analyses of fasting plasma concentrations of insulin and glucose, and serum lipids and lipoproteins.7 Twenty-four-hour ABPMs were completed in 950 of the participants in the cognitive study, using the Accutrack 2 equipment (Suntech Medical Instruments Inc). BP recordings were made every 20 minutes during daytime (6:00 AM to 11:00 PM) and every 20 or 60 minutes during nighttime (11:00 PM to 6:00 AM). The following variables were used...
Selected Abbreviations and Acronyms

ABPM = ambulatory blood pressure measurement  
BMI = body mass index  
BP = blood pressure  
DBP = office diastolic blood pressure  
DDBP = mean daytime diastolic blood pressure  
DSBP = mean daytime systolic blood pressure  
HR = heart rate  
ICD = International Classification of Diseases  
MAP = mean arterial pressure  
M/I = insulin sensitivity index  
MMSE = Mini-Mental State Examination  
NBP = nocturnal blood pressure  
NDBP = mean nocturnal diastolic blood pressure  
NSBP = mean nocturnal systolic blood pressure  
OGTT = oral glucose tolerance test  
SBP = office systolic diastolic blood pressure  
TMT = Trail-Making Test

Cognitive Function

The psychometric testing included the MMSE (n=891) (MMSE was added to the protocol after the start) and the TMT-A (n=998) and TMT-B (n=996). Standardized procedures from published manuals were used in the administration and evaluation. The maximal time set for TMT-B was 240 seconds. MMSE is a widely used instrument in the screening for cognitive disorders, and the TMT was selected to assess psychomotor speed and shifting capacity. The testing was performed in connection with the ABPM in some cases, but in others the time interval was longer (mean, 18 months). After a logarithmic transformation of the test results, a z transformation was applied, and a composite cognitive score was calculated for each subject as the mean sum of the test scores. Cognitive score was treated both as a continuous outcome variable and as a dichotomous variable, setting the cutoff level for low results at the lowest quintile.

Potential Confounders

All pharmacological treatment with agents affecting BP, irrespective of indication (ie, β-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors, diuretics, and α-blockers), was recorded in a questionnaire at age 70 years. Educational level was stratified as low (elementary school only, 6 to 7 years, n=530), medium (secondary school, n=309), or high (university studies, n=160). Main previous occupational level was divided into three categories: low (manual workers, n=406), medium (foremen, clerks, salesmen, n=388), and high (major professionals, business managers, n=193). The following are diagnoses of stroke according to the ICD-8 or ICD-9 before the cognitive testing results were collected from the Swedish National Inpatient Register and cover all diagnoses in hospitalized patients from 1970 and onward: intracerebral hemorrhage (431), thromboembolic stroke (433 to 434), transient ischemic attack (435), and acute “ill-defined” cerebrovascular disease (436). Informed consent was obtained from the participants after the nature of the procedures had been fully explained. The study was approved by the Ethics Committee at Uppsala University.

Statistics

A logarithmic transformation was applied to all variables not normally distributed. Student’s unpaired t test was applied for comparisons between independent groups, the χ² test was used for analysis of relationships between categorical variables, and linear relationships were examined with Pearson’s correlation coefficient. In the analyses of determinants of cognitive function, adjustment was made for potential confounders, ie, socioeconomic factors (educational and occupational levels) and age. ANCOVA was applied in multivariate models with continuous dependent variables, and logistic regression was used when the outcome variable was binary. The odds ratio for continuous explaining variables was calculated per increase with 1 SD within a 95% confidence interval or per year (age). Testing for trend was performed according to Spearman.

Results

Description of the Population

Characteristics of the participants (n=999) are shown in Table 1. Diabetes according to the OGTT was present in 139 subjects (14.2%), and a total of 5.3% were treated with peroral antidiabetic agents or insulin. Thirty-four percent were treated with drugs affecting BP, irrespective of indication, mainly β-blockers and/or diuretics (26%), and the rate of treatment with lipid-lowering agents was 9.4%. The correlation coefficient between MMSE and TMT-A was r=.32; between MMSE and TMT-B it was r=.40; and between TMT-A and TMT-B it was r=.66. Seventy men had had a previous stroke, and they were excluded from the main part of the analyses. Excluding stroke patients, a large majority had high scores in the MMSE. 462 men scored 29 to 30 points; 287 men scored 27 to 28 points, and 77 men scored 26 points or below. The nonparticipants in the cognitive testing (n=222) differed from the participants (n=999) with regard to a higher rate of low

### Table 1. Description of Participants (n=999)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage/ Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education ≤7 y</td>
<td>53.1%</td>
</tr>
<tr>
<td>Low occupational level</td>
<td>41.2%</td>
</tr>
<tr>
<td>50-Year survey</td>
<td></td>
</tr>
<tr>
<td>Office DBP, mm Hg</td>
<td>82 (10)</td>
</tr>
<tr>
<td>s-Glucose, mmol/L</td>
<td>5.0 (0.6)</td>
</tr>
<tr>
<td>s-Inulin (ml/L)</td>
<td>12.4 (6.8)</td>
</tr>
<tr>
<td>70-Year Survey</td>
<td></td>
</tr>
<tr>
<td>24-h DBP, mm Hg</td>
<td>76 (8)</td>
</tr>
<tr>
<td>Nondippers*</td>
<td>6.8%</td>
</tr>
<tr>
<td>p-Glucose, mmol/L</td>
<td>5.8 (1.5)</td>
</tr>
<tr>
<td>p-Inulin, ml/L</td>
<td>12.8 (8.4)</td>
</tr>
<tr>
<td>M/I</td>
<td>5.1 (2.5)</td>
</tr>
<tr>
<td>s-Triglycerides, mmol/L</td>
<td>1.43 (0.78)</td>
</tr>
<tr>
<td>M/I</td>
<td>26.3 (3.3)</td>
</tr>
<tr>
<td>Diabetes (OGTT)</td>
<td>14.2%</td>
</tr>
<tr>
<td>Antihypertensive treatment†</td>
<td>34.2%</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>7.0%</td>
</tr>
</tbody>
</table>

* Nondippers indicate SBP daytime minus SBP nighttime ≤0 mm Hg.† Any pharmacological treatment affecting BP.
education (72%, $P<.0001$ compared with participants). In addition, they had higher office DBP at age 50 and higher plasma concentrations of insulin at age 70 (both $P<.05$). The distributions of 24-hour DBP were equal in participants and nonparticipants.

**Interrelationships Between Risk Factors**

The correlation coefficients between office and 24-hour measurements were $r=.58$ for SBP and $r=.62$ for DBP. There were only weak linear relationships between BP and metabolic measurements. The correlation coefficients between metabolic measurements and 24-hour DBP were as follows: plasma glucose, $r=.12$ ($P=.003$); plasma insulin, $r=.08$ ($P=.05$); M/I, $r=-.12$ ($P=.003$); and BMI, $r=.13$ ($P=.0007$). Serum lipids were not significantly related to 24-hour DBP. Concentrations of serum triglycerides were closely related to M/I ($r=-.39$) and to plasma glucose ($r=.27$). Plasma glucose was significantly higher in nondippers (6.3 mmol/L) than in dippers (5.7 mmol/L), independent of 24-hour DBP ($P=.008$, logistic regression).

**Vascular Risk Factors and Cognitive Function**

The mean cognitive $z$ score in the entire cohort was $±0.00$ (SD 0.82; range, $-5.19$ to $+2.00$). Cognitive score was equal in men with missing results from the ABPM, the clamp, or the OGTT compared with the others. Stroke patients ($n=70$) were excluded from the analyses of determinants of cognitive function. Their results are shown separately. In all analyses, adjustment was made for age and educational and occupational levels. The relationships with the composite cognitive score described below were unchanged when separate analyses between risk factors and the single test results (MMSE, TMT-A, TMT-B) were performed.

**Longitudinal Measurements**

Office DBP at baseline (age 50) was inversely related to cognitive function 20 years later. In the analysis, participants were split into five DBP categories. Cognitive performance at age 70 was highest in men with the lowest baseline BP, DBP $≤70$ mm Hg ($n=147$), and lowest in men with DBP $≥105$ mm Hg ($n=36$), adjusted value for trend $P=.0040$ (Table 2). Rates of antihypertensive treatment and office DBP at age 60 and 70 years in each BP category are also shown in Table 2. Only 3 men with DBP $≥105$ mm Hg were not treated 20 years later; their mean cognitive score was $-1.24$. Serum concentrations of insulin at age 50 were also inversely related to cognitive results at follow-up (Fig 1). Men within the lowest tertile of $s$-insulin had higher results than those in the highest tertile; the difference was, however, not significant when DBP was adjusted for. High systolic BP, BMI, or high levels of blood glucose or serum lipids at baseline were not associated with later impaired performance.

**Cross-sectional Measurements**

**Blood Pressure**

There was an inverse relationship between 24-hour ambulatory SBP and DBP at age 70 years and cognitive score, NDBP showing the strongest linear relationship ($r=-.15$, $P=.0001$). Mean HR during 24 hours was also inversely related to cognitive $z$ score ($r=-.12$, $P=.0015$). Cognitive score by tertiles of 24-hour DBP are shown in Fig 2, with separate analyses for untreated men ($n=594$) and treated men ($n=289$). The inverse relationship between BP and cognitive score was similar in both categories but significant for untreated men only ($P=.014$ for trend). Mean cognitive score did not differ between men with and without treatment ($±0.03$ versus $±0.02$, respectively, $P=.941$), despite higher mean 24-hour DBP in the latter group (75 versus 78 mm Hg, respectively, $P<.0001$). This finding is discussed further in the following sections. Isolated systolic hypertension was not related to impaired cognitive function.

**Nondipping and BP Variability**

Mean cognitive score was lower in nondippers ($n=59$, $-0.22$, SD 0.95), than in dippers ($n=824$, $+0.04$ [0.77], $P=.04$). In multivariate analyses with cognitive score as a continuous outcome variable, nondipping, mean 24-hour DBP, and mean 24-hour HR were all significantly and inversely related to cognitive score ($P<.01$). Cognitive score in tertile 1 versus tertile $3$, ANCOVA; $P^2$ (adjusted for age, education, occupation) $=.031$; $P^2$ (as $P^2$+DBP at age 50) $=.145$.

**Table 2. DBP at Age 50 Years in Relation to Cognitive Function at Age 70 Years**

<table>
<thead>
<tr>
<th>DBP at Age 50 y</th>
<th>Cognitive score, Mean (SD)</th>
<th>$P^*$</th>
<th>Treatment at 60 y</th>
<th>DBP at 60 y</th>
<th>Treatment at 70 y</th>
<th>DBP at 70 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>$≤70$ mm Hg ($n=147$)</td>
<td>$+0.17$ (0.71)</td>
<td>. .</td>
<td>2.7%</td>
<td>78 (7)</td>
<td>8.2%</td>
<td>79 (10)</td>
</tr>
<tr>
<td>75–80 mm Hg ($n=392$)</td>
<td>$±0.00$ (0.82)</td>
<td>.0065</td>
<td>2.8%</td>
<td>85 (8)</td>
<td>23.2%</td>
<td>82 (9)</td>
</tr>
<tr>
<td>85–90 mm Hg ($n=268$)</td>
<td>$+0.04$ (0.70)</td>
<td>.0018</td>
<td>17.2%</td>
<td>90 (8)</td>
<td>39.9%</td>
<td>86 (9)</td>
</tr>
<tr>
<td>95–100 mm Hg ($n=86$)</td>
<td>$±0.00$ (0.89)</td>
<td>.032</td>
<td>51.2%</td>
<td>95 (9)</td>
<td>70.9%</td>
<td>89 (9)</td>
</tr>
<tr>
<td>$≥105$ mm Hg ($n=36$)</td>
<td>$-0.33$ (0.82)</td>
<td>.0016</td>
<td>88.9%</td>
<td>96 (8)</td>
<td>91.7%</td>
<td>89 (9)</td>
</tr>
</tbody>
</table>

$^*$Comparisons with DBP $≤70$ mm Hg, adjusted for age and educational and occupational levels. Test for trend: $P=.0040$; $P=.034$, including serum insulin at age 50.
cognitive performance, independent of each other. Cognitive performance in men with high NBP variability as measured by the quotient between SD (of NSBP) divided by mean (of NSBP), and in extreme dippers ($D[DSBP-NSBP]$ of $\geq 20$ mm Hg), was equal to the rest of the cohort. There was no relationship between the number of missing single measurements due to technical reasons and cognitive performance.

**Insulin Resistance and Diabetes**

As shown in Fig 3, measurements of M/I was negatively related to cognitive results ($P=0.048$ for trend). When adjustment was made for 24-hour DBP and treatment, the value for trend was $P=0.055$. Men with diabetes according to the OGTT ($n=130$) performed worse than nondiabetic men ($n=779$, 0.16 [0.90] versus 0.06 [0.75]), independent of 24-hour DBP ($P=0.005$). In a multivariate model ($n=868$), diabetes, nondipping, and 24-hour DBP were all independently and inversely related to cognitive score as a continuous outcome variable. In diabetic men, performance was equal in men with and without pharmacological treatment. Stratifying for diabetics did not alter the relationship between high DBP and low cognitive results.

**Multivariate Analysis**

In a logistic regression model, cognitive function was treated as a dichotomous variable with the cutoff level for low performance set at the lowest quintile. In univariate analysis, men with low cognitive function had higher 24-hour DBP and higher plasma glucose (Table 3). In a multivariate model that included 24-hour DBP, $p$-glucose, $p$-insulin, M/I, $s$-triglycerides, BMI, HDL cholesterol, treatment, age, educational and occupational levels, an increase of 24-hour DBP with 1 SD was associated with an odds ratio of 1.45 (1.20 to 1.75) of cognitive impairment. Despite higher DBP in treated men, antihypertensive treatment was associated with a decreased risk, i.e., treatment was a negative confounder. As shown in Table 4, the association between hypertension and cognitive impairment was significant only in untreated men.

**Stroke Patients**

Men with a previous stroke ($n=70$) had lower cognitive results; mean cognitive score (SD) was -0.43 (1.14) versus -0.02 (0.78) for nonstroke subjects ($P=0.0001$), and they had higher DBP at baseline. When stroke cases were included in the analyses previously described, the relationships between vascular risk factors and low cognitive performance remained almost identical.

**Discussion**

High DBP at the baseline examination at age 50 years was related to impaired cognitive performance 20 years later, even after exclusion of men with a previous stroke. Elevated concentrations of serum insulin also predicted low cognitive function, but not independently of DBP. Cross-sectional measurements at age 70 showed that high 24-hour DBP, a nondipping nocturnal BP pattern, insulin resistance, and diabetes all were related to low cognitive function. The relationships between hypertension and cognitive impairment were strongest in men without antihypertensive treatment. High BP and impaired glucose metabolism are both independent predictors of cerebrovascular disease. We conclude that hypertension and factors linked to the syndrome of insulin resistance might contribute to cognitive disturbances in the elderly, mediated through functional changes, or by silent cerebral large- and small-vessel lesions.

This group was a healthy cohort in which only a minority of the participants scored below 27 points in the MMSE. It consisted of approximately half of the survivors from the baseline examination only, but nonresponse to health surveys has, on the other hand, been shown to be associated both with
a higher vascular risk and with cognitive impairment. Those who declined to participate in the cognitive testing had a lower level of education and higher office BP and serum insulin than the participants, ie, factors with positive relationship to the outcome. Furthermore, in our study cohort, the risk factor pattern has been blunted not only by selection but also by the effects of preventive treatment. Special efforts to prevent cardiovascular disease were taken since the 50-year survey, in which primary preventive measures were instituted in men who were found to be hypertensive, hyperlipidemic, or had an impaired glucose tolerance. Thus, we believe that the inference of the relationships to the general population of community-living elderly males might rather be underestimated.

The most convincing evidence of a relationship between hypertension and cognitive deterioration is derived from a prospective study in the 1960s, when antihypertensive treatment was still infrequent. The authors suggested that "the basis for the cognitive decline associated with aging should be considered secondary to some pathologic processes and not merely as a 'normal' aging process." Results from other studies assessing longitudinally measured BP point in the same direction. In the Honolulu–Asia Aging Study, high midlife SBP was a predictor of reduced cognitive function in later life, when stroke cases were included. In the Framingham study, untreated BP levels and chronicity of hypertension were inversely related to the composite cognitive score. Diabetes in the elderly has been linked to cognitive impairment in cross-sectional case-control studies, and impaired cognitive performance in diabetic subjects has been related to poorer metabolic control. In other studies, the combinations of hypertension and hyperinsulinemia, hypercholesterolemia, or diabetes, as defined by a

TABLE 3. Determinants of Low Cognitive Performance: Cross-sectional Data at Age 70 Years

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cognitive Function</th>
<th>Logistic Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (n=1068)</td>
<td>Low (n=186)</td>
</tr>
<tr>
<td>24-h DBP, mm Hg</td>
<td>76 (8)</td>
<td>78 (8)</td>
</tr>
<tr>
<td>IP-Glucose, mmol/L</td>
<td>5.7 (1.4)</td>
<td>6.0 (1.8)</td>
</tr>
<tr>
<td>IP-Insulin, mU/L</td>
<td>12.7 (8.2)</td>
<td>13.3 (9.2)</td>
</tr>
<tr>
<td>M/I</td>
<td>5.2 (2.5)</td>
<td>4.8 (2.6)</td>
</tr>
<tr>
<td>IS-Triglycerides, mmol/L</td>
<td>1.39 (0.71)</td>
<td>1.57 (1.04)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.1 (3.2)</td>
<td>26.9 (3.9)</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.30 (0.34)</td>
<td>1.25 (0.37)</td>
</tr>
<tr>
<td>Antihypertensive treatment, %</td>
<td>32.6</td>
<td>33.3</td>
</tr>
<tr>
<td>Age, y</td>
<td>72.3</td>
<td>72.8</td>
</tr>
<tr>
<td>Education, L/M/H</td>
<td>46/35/19%</td>
<td>81/15/4%</td>
</tr>
<tr>
<td>Occupation, L/M/H</td>
<td>35/42/23%</td>
<td>66/30/4%</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD). Low function indicates cognitive score within the lowest quintile; OR, odds ratio; CI, 95% confidence interval; and L/M/H, low/medium/high.

P1 model includes age, educational, and occupational levels (ANCOVA). OR and CI for continuous variables are calculated per 1 SD increase (per 1 year for age). All listed covariates are included in the logistic regression model.

TABLE 4. Determinants of Low Cognitive Performance Stratified for Antihypertensive Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Untreated Men</th>
<th>Treated Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cognitive Performance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal (n=1068)</td>
<td>Low (n=186)</td>
</tr>
<tr>
<td>24-h DBP, mm Hg</td>
<td>75 (7)</td>
<td>78 (8)</td>
</tr>
<tr>
<td>IP-Glucose, mmol/L</td>
<td>5.6 (1.3)</td>
<td>5.8 (1.7)</td>
</tr>
<tr>
<td>IP-Insulin, mU/L</td>
<td>12.4 (8.8)</td>
<td>11.9 (7.5)</td>
</tr>
<tr>
<td>M/I</td>
<td>5.6 (2.5)</td>
<td>5.1 (2.7)</td>
</tr>
<tr>
<td>IS-Triglycerides (mmol/L)</td>
<td>1.33 (0.65)</td>
<td>1.46 (1.04)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.6 (2.9)</td>
<td>26.5 (4.0)</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.33 (0.35)</td>
<td>1.28 (0.36)</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD). Low function indicates cognitive score within the lowest quintile.

*Adjusted for age, education, and occupation (ANCOVA).
questionnaire, were related to impaired cognitive function. To our knowledge, ours is the first cohort study showing that cognitive impairment is related to metabolic disturbances linked to the syndrome of insulin resistance, together with hypertension.

The finding that diastolic BP in middle age predicts later cognitive performance suggests a causal relationship. However, the data from the ABPM are cross-sectional, and causal mechanisms can only remain speculative. The causation might be reverse, ie, cognitive impairment and altered BP regulation may both be secondary to silent cerebrovascular lesions. In cross-sectional studies, silent lacunar infarctions and vascular dementia characterized by extensive white matter lesions or by multiple lacunar infarctions have been related to the absence of NBP decrements. Changes in BP circadian variability indicate alterations of central nervous regulatory systems, mediated by sympathetic activation. However, on the other hand, sympathetic overreactivity could also be etiologically linked to the syndrome of hypertension and insulin resistance, and primarily affect cognitive function by vasoconstriction and cerebral small-vessel lesions. The TMT reflects subcortical-frontal functions, among others, and impaired performance in the TMT has previously been associated with subcortical small-vessel lesions. Is low BP always desirable, or is there a lower limit below which too-aggressive antihypertensive treatment might be hazardous? It has been hypothesized that low systemic BP might primarily contribute to dementia via impaired cerebral perfusion and incomplete white matter infarctions in areas supported by stenosed vessels. Extreme dipping, as well as nondipping, was associated with silent cerebrovascular disease identified by magnetic resonance imaging. Moderate or severe dementia is accompanied by lower BP levels, but in advanced stages, this is most likely a secondary phenomenon. A previous study showed that cognitive changes in hypertensive subjects, hypothetically mediated through metabolic or hemodynamic mechanisms, could be restored by treatment. In our cohort, there existed no J-shaped relationship between BP and cognitive function, and there were also indications of a positive effect of treatment. This latter finding should be interpreted with caution, because it may be due to selection.

To summarize, our results support the hypothesis that cerebral target-organ damage in hypertension contributes to cognitive impairment. Cognitive deterioration denotes an impaired quality of life and is also a predictor of dementia and mortality. Actions to prevent further decline must be considered as early in the course of the disease as possible, ie, before clinical manifest dementia. Because a linkage with risk factors for vascular disease has been established, it is urgent to investigate whether further cognitive decline can be postponed by a more intensive preventive treatment. There is convincing evidence of the importance of adequate antihypertensive treatment in primary prevention of cerebrovascular disease even in higher ages, and there are no indications of treatment causing cognitive deterioration. Our findings suggest that treatment with pharmacological agents that maintain the normal 24-hour BP profile and have no metabolic side effects should be preferred in the management of elderly persons with hypertension.

Acknowledgments

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References


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