Circadian Blood Pressure Pattern and Cognitive Function in Middle-aged Essential Hypertensive Patients

Patrón circadiano de la presión arterial y función cognitiva de pacientes de mediana edad con hipertensión esencial

To the Editor,

Several studies have shown a relationship between hypertension and cognitive impairment, especially in elderly people. However, data on the relationship between the circadian blood pressure (BP) pattern and cognitive function are conflicting. Differences among studies could be due to sample characteristics: most participants were elderly, diabetic, had previous history of cardiovascular disease, or were undergoing antihypertensive therapy, which could influence their cognitive status. This study investigated the relationship between the circadian BP pattern and cognitive function in a homogeneous sample of asymptomatic, middle-aged, never-treated essential hypertensive patients.

Fifty-six never-treated essential hypertensive patients (37 men), aged 50-60 years (mean [SD] age 54.3 ± 3.1 years) without clinical evidence of target organ damage were consecutively selected from the Hypertension Unit of Hospital Clinic, Barcelona, Spain. Exclusion criteria included type 2 diabetes mellitus (fasting plasma glucose > 6.6 mmol/L), carotid stenosis > 50% measured by ultrasonography, alcohol intake > 30 g of pure ethanol per day, sleep apnea syndrome, clinical evidence of cerebrovascular or coronary heart diseases, cardiac failure, atrial fibrillation, papilledema, and renal impairment (serum creatinine > 115 μmol/L).

All patients underwent 24-hour ambulatory BP monitoring. The nocturnal drop in BP was calculated as the difference between average daytime and nighttime systolic BP (SBP) values.

Cognitive function was evaluated by a battery of neuropsychological tests that included an Intelligence Quotient estimation (Vocabulary and the Kohs block design subtests of the Spanish adaptation of the Wechsler Adult Intelligence Scale), tests of attention and working memory (Digit Forward and Backward Span test, respectively, from the Wechsler Adult Intelligence Scale-Revised), and tests for evaluating memory (the Russell Revision of the Logical Memory subscale and the Visual Reproduction subscale of the Wechsler Memory Scale).

Thirty-four hypertensive patients were found to be nondippers (nocturnal SBP fall less than 10%). The main baseline characteristics, including age, sex distribution, body mass index, serum fasting glucose, lipid profile, renal function, duration of hypertension, and smoking status did not differ between these 2 groups. Nondippers had significantly higher values of nighttime SBP and diastolic BP than dippers (Table 1).

In the neuropsychological evaluation, no differences in intelligence, education, or anxiety or depression scales were observed between the 2 groups. Nondippers had lower scores on the working memory test and the logical memory test than dippers but this difference was not statistically significant (Table 2). Nondipper hypertensive patients performed significantly worse on the visual memory test than dippers. This association remained significant (P = .033) after adjustment for 24-hour SBP and diastolic BP values, and also for age and level of education (P = .029). In addition, we found a significant correlation between the nocturnal drop in SBP and better performance on the visual memory test (r: 0.407; P = .003).

This study shows an association between the presence of nondipping BP status and worse performance on the visual memory test. In addition, there was a significant correlation between the nocturnal drop in SBP and better performance on the visual memory test. Kilander et al. reported in 999 patients aged 70 years old that the mean cognitive score was lower in nondippers than in dippers. In this study, cognitive function was mainly assessed by the Mini-Mental State examination, and some of the individuals were diabetic or had a previous history of stroke. In the present study, cognitive function was assessed by means of a battery of neuropsychological tests that is more sensitive to early or subtle cognitive impairment than the Mini-Mental State examination. It is known that age-related cognitive decline is more pronounced in speed performance functions than in verbal or visual spatial tests. High BP seems to first alter memory domains, such as visual reproductions-immediate and delayed recall. Kawas et al. showed that poor visual memory performance may represent an early expression of Alzheimer disease years before diagnosis. However, it is unclear whether the mild disturbance in the visual memory test may represent the skills most susceptible to disruption and those that decline first as a result of high BP.

### Table 1

<table>
<thead>
<tr>
<th>Twenty-four-hour Blood Pressure Values</th>
<th>Dippers</th>
<th>Nondippers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-h SBP, mmHg</td>
<td>137.8 (18.1)</td>
<td>144.2 (12.4)</td>
<td>.087</td>
</tr>
<tr>
<td>Daytime SBP, mmHg</td>
<td>143.4 (18.1)</td>
<td>147.3 (12.7)</td>
<td>.366</td>
</tr>
<tr>
<td>Nighttime SBP, mmHg</td>
<td>124.9 (17.7)</td>
<td>141.2 (12.4)</td>
<td>.001</td>
</tr>
<tr>
<td>24-h DBP, mmHg</td>
<td>86.8 (10.7)</td>
<td>92.1 (9.7)</td>
<td>.031</td>
</tr>
<tr>
<td>Daytime DBP, mmHg</td>
<td>90.8 (10.7)</td>
<td>94.6 (9.6)</td>
<td>.161</td>
</tr>
<tr>
<td>Nighttime DBP, mmHg</td>
<td>77.3 (11.0)</td>
<td>87.0 (10.6)</td>
<td>.001</td>
</tr>
</tbody>
</table>

DBP, diastolic blood pressure; SBP, systolic blood pressure. Values are expressed as mean (standard deviation).
This study has some limitations related to methodological aspects. The study has a cross-sectional design and a small sample size. A causal mechanism between diminished nocturnal SBP fall and lower cognitive performance can only remain speculative.

The strengths of this study include the relatively young study population in an attempt to address the relationship between the circadian BP pattern and cognitive function at early stages. Indeed, because aging and associated factors may influence cognitive performance, the present study included a homogeneous sample of middle-aged essential hypertensive patients, who never received antihypertensive treatment, without a history of cardiovascular disease, and excluded those with established risk factors for the development of cerebrovascular damage such as diabetes or significant alcohol intake.

The mechanisms underlying hypertension-related cognitive changes are complex and are not yet fully understood. It has been suggested that increased BP may increase the risk of cognitive impairment or dementia involving small-vessel disease. With respect to the circadian BP pattern, it has been reported in elderly hypertensive patients that nondippers had significantly more silent cerebrovascular damage (measuring both lacunae infarct and white matter lesions) than dippers.

The mechanism of nocturnal BP dipping is still largely unknown, but reduced sympathetic nervous activity during the night may be a contributory factor. Possible mechanisms relating the nondipping pattern with the development of cognitive impairment are purely speculative. However, as has been suggested to occur after a clinical stroke and in cerebral lacunae infarcts, an imbalance between sympathetic and parasympathetic activities during the nighttime may contribute to the pathogenesis of cerebral damage in hypertension, in addition to the severity of high BP.

The underlying mechanism that connects a blunted reduction in BP during the night with cognitive impairment remains to be determined, and longitudinal studies are necessary.

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**REFERENCES**


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Table 2
Neuropsychological Results of Dipper and Nondipper Hypertensive Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dippers</th>
<th>Nondippers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit span WAIS-R forward</td>
<td>4.95 (1.05)</td>
<td>5.0 (1.15)</td>
<td>.752</td>
</tr>
<tr>
<td>Working memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit span WAIS-R backward</td>
<td>4.25 (0.81)</td>
<td>4.00 (0.87)</td>
<td>.432</td>
</tr>
<tr>
<td>Memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logical memory, recall after delay, %</td>
<td>84.6 (13.2)</td>
<td>80.1 (16.7)</td>
<td>.311</td>
</tr>
<tr>
<td>Visual reproduction, recall after delay, %</td>
<td>94.5 (11.9)</td>
<td>83.9 (19.1)</td>
<td>.017</td>
</tr>
</tbody>
</table>

WAS-R. Wechsler Adult Intelligence Scale-Revised.
Values are expressed as mean (standard deviation).

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