Relationship Between Blood Pressure and Subcortical Lesions in Healthy Elderly People

Iris B. Goldstein, PhD; George Bartzokis, MD; Darwood B. Hance, MD; David Shapiro, PhD

Background and Purpose—The relationship between blood pressure (BP) and heart rate (HR) and MRI assessments of subcortical T2 hyperintensities was evaluated in healthy elderly men and women.

Methods—Casual and 24-hour ambulatory BPs and HR measurements were taken of 144 elderly individuals, aged 55 to 79 years. Subjects had no evidence of previous health disorders. MRI scans of white matter, subcortical gray matter, and insular subcortex were coded for severity of hyperintensities.

Results—Mean casual BP for the group was 120/72 mm Hg. With age and sex accounted for, individuals with the highest severity rating of white matter hyperintensities had higher casual, awake, and sleep systolic BPs; higher awake diastolic BPs; greater awake systolic BP variability; and a smaller nocturnal fall in systolic and diastolic BPs than individuals with less severe ratings. Higher severity ratings for subcortical gray matter hyperintensities were associated with elevations in casual, awake, and asleep systolic BPs and a smaller HR drop during sleep. Subjects with higher ratings for the insular subcortex had higher systolic and diastolic BPs (casual, awake, and asleep), greater HR variability during sleep, and a smaller nocturnal fall in HR.

Conclusions—Casual and 24-hour ambulatory BPs and some ambulatory HR measures are associated with subcortical lesions of the brain. Longitudinal studies are needed to further explore the relationship between white matter lesions and cardiovascular measures, as well as the significance of these lesions for cerebrovascular disease in healthy elderly subjects. (Stroke. 1998;29:765-772.)

Key Words: blood pressure ■ elderly ■ heart rate ■ magnetic resonance imaging

The single most important risk factor for cardiovascular and cerebrovascular disease for all age groups is BP. Investigators have shown that particularly among the elderly hypertensive patients have a relatively high incidence of lacunar infarcts and white matter hyperintensities when compared with normotensive subjects. However, it may not be necessary for BP to be in the hypertensive range for it to be considered a risk factor. Data from insurance studies indicate that there is a gradient of ratios of actual to expected mortality that increases with elevations in SBP. Even in nonhypertensive individuals 19 to 91 years of age, higher casual SBP was associated with a greater volume of white matter HI.

Most BP information on the elderly has been obtained by means of standard clinic BP assessment. However, with the aid of 24-hour ambulatory monitoring one can track BP during both awake and sleep periods and obtain information on BP variability and falls in nocturnal BP. For example, in a study of elderly subjects who had either never been on antihypertensive medication or had not been taking it for 4 weeks, MRI abnormalities were associated with elevated ambulatory BP, a small nocturnal fall in BP, and a lower HR.

Using both casual and ambulatory assessments in the present study, we evaluated the relationship between BP and HR and T2 HI in 144 healthy, active, unmedicated elderly men and women with no evidence of previous BP, cardiovascular, psychological, or neurological disorders.

Subjects and Methods

Subjects were recruited by media advertisements and from senior centers in Los Angeles. Potential participants had to be healthy men and women aged 55 to 80 years who were living in the community. From a total of 1154 people inquiring about the study, 187 were not interested and 758 did not meet the criteria. Fifty-nine subjects were dropped after the medical examination, 3 were later dropped for noncompliance, and MRIs could not be obtained for 3 subjects. The final sample consisted of 144 subjects. All subjects gave informed consent, with approval obtained from the Human Subjects Protection Committee of the University of California, Los Angeles. Eligible subjects underwent medical examinations and were scheduled to begin ambulatory BP monitoring a few days later. They were studied during two 24-hour time periods, on weekdays, about a week apart. At the end of the procedures MRIs were recorded. Procedures are elaborated below.

Initial Screening

All subjects went through extensive screening, beginning with telephone contact. Initial exclusions involved subjects’ reports of any serious current or prior illness, history of hypertension, drug or alcohol abuse, head injuries, obesity (body mass index >30 kg/m²),
prior psychiatric illness, or any medications influencing either the cardiovascular or central nervous system. We also excluded anyone who had first-degree relatives with Alzheimer’s disease, schizophrenia, or Huntington’s chorea.

Medical Evaluation and Final Screening
On their first visit, subjects were given a physical and mental status examination by the project physician, including a complete health history, 12-lead ECG, urinalysis, and chemical panel. Laboratory tests were done by standard techniques (SmithKline Beecham Clinical Laboratories). Exclusion criteria included neurological (eg, history of cerebrovascular accident, Parkinson’s disease, or any serious involvement of the central nervous system), cardiovascular (eg, congestive heart failure, myocardial infarction, history of coronary disease, atrial fibrillation, or symptomatic ventricular arrhythmias), respiratory (eg, symptomatic bronchospastic diseases), renal (eg, elevated creatinine; proteinuria), endocrine, and major psychiatric or other disorders. Those with possible diabetes (fasting glucose of >115 mg/dL or a glucose >200 mg/dL after 1 hour or >114 mg/dL after 2 hours of a glucose tolerance test with 75 g of glucose) were also excluded. Exclusions were based on medical examination, laboratory findings, and subject’s medical history.

The Mini Mental State Examination15 screened out cognitive disorders (scores of <23), and the Brief Symptom Inventory16 screened out individuals with possible psychiatric symptoms. Subjects scoring >5 on the short form of the Geriatric Depression Scale17 were also excluded. The Spielberger Trait Anxiety Scale18 was administered to use as a covariate in later analyses.

Ambulatory Monitoring
The Accutracker II (Sintech Medical Instruments) was used for 24-hour ambulatory BP monitoring. It has been used widely in clinical and research studies and has established reliability and validity.13 After the subject was seated for 5 minutes and just before the ambulatory monitor hookup, we assessed casual BP and HR. Three successive readings of BP were taken according to standard assessments.14 Three readings were also taken of radial pulse rate. The laboratory assistant then applied the ambulatory monitoring cuff to the nondominant arm. On each measurement occasion, single readings of SBP and DBP were obtained.13 The ambulatory recorder was programmed to operate three times an hour on a random schedule during waking hours and once an hour during sleep. Actual time of awake and sleep periods was noted in subject’s diary. On the basis of the subject’s information, we obtained indices of quality of sleep, number of times awakened, and number of hours slept. The Epworth Sleepiness Scale was administered to assess the presence of daytime sleepiness. This scale has also been found to significantly distinguish normal subjects from patients with sleep disorders (ie, sleep apnea syndrome) identified by polysomnography.16 Ambulatory data were first edited for artifact based on Accutracker reading codes (insufficient ECG or Korotkoff sounds) and extreme values (>200/120 or <70/40 mm Hg). Editing was done entirely by set rules.12 Far outside values were excluded by the box plot program of Systat. For each subject ambulatory measures for SBP and DBP included mean values of awake and sleep periods. Classification of each reading as awake or asleep was based on diary entries and post-session reports. Only nighttime sleep values were included in the sleep category.

In addition to averaging casual BP and HR for 2 days, mean values for the following ambulatory measures were averaged over two 24-hour time periods: awake level, asleep level, awake variability, asleep variability, and percent drop during sleep. Change in BP or HR from awake to sleep divided by the awake value [(awake–asleep)/awake] represented percent drop. For a given subject, variability was based on the standard deviation of the awake and of the asleep periods for a given day. All data were based on a single day and averaged over 2 days.

Activity Monitor
An actigraph (Mini-Motionlogger, Ambulatory Monitoring Inc) was used to record frequency of movements in 1-minute intervals during each 24-hour period of ambulatory monitoring. Using a custom computer program (prepared by Timothy Elsmore, PhD), we obtained measures of the average activity level for sleep and for awake periods and for the 10-minute period preceding each BP reading. The activity monitor was used to confirm the differentiation of asleep from awake readings and to account for the effects of activity on BP and HR.

MRI Evaluation

Imaging Protocol
MRI was performed using a Picker 1.5T instrument with an imaging protocol consisting of four sequences. The initial spin-echo sequence (TR, 100 msec; TE, 30 msec; 10 mm thickness) of a coronal pilot image with one signal averaged was used to evaluate symmetrical positioning of the head. If a subject’s head was tilted noticeably laterally, the subject was repositioned and a new coronal pilot image was acquired. The image was then used to align the acquisition grid of the subsequent sagittal images. Pilot sagittal images were obtained from a second spin-echo sequence (TR, 550 msec; TE, 26 msec; 5 mm thickness) with two signals averaged. To obtain a true midsagittal image, the middle slice of this series of 28 images was aligned on the coronal pilot.17 The remaining sagittal images visualized the entire brain, and were used to determine the position of the two subsequent axial sequences in order to image the entire brain in the axial plane from the apex to the inferior ends of the temporal lobes. A transverse dual spin-echo sequence (TR, 2500 msec; TE, 20 and 90 msec) with 256×192 view matrix, 25-cm field of view, and two signals averaged was used to acquire the 3-mm-thick contiguous axial images used in the ratings of HI. This sequence was performed twice to visualize the entire brain.

MRI Ratings
The images were rated visually for areas of HI by two of us (D.H. and G.B.), both blinded to other research data on the subjects. Ratings of T2 HI were made without regard to clinical significance, and only HI identified on both early and late echo images were rated. In the evaluation of focal HI the raters selected abnormal foci and avoided including expected HI, such as those produced by partial voluming of sulcal cerebrospinal fluid or uniform round cortical vessels appearing in typically anticipated positions within sulci. Interobserver reliability was tested by rerating a subset of 27 scans and comparing the results of two independent raters. Intraclass correlation coefficients were computed by estimating variance components associated with between-subject and within-subject variabilities. The coefficients reflect the proportion of total variance accounted for by differences among subjects. Significance of the intraclass correlations was determined by the general linear model, with subjects forming the grouping factor. Reliability coefficients (intraclass r) were highly significant (P<.0001) for HI severity ratings for the three regions: white matter (r=.90, F=18.6); insula (r=.85, F=12.3); and subcortical gray matter (r=.88, F=16.3).

Subjects’ scans of HI of white matter, subcortical gray matter (basal ganglia and thalamus), and insular subcortex were all rated on the basis of intensity, size, and confluence of lesions. The absence of HI in a particular brain region was rated as zero. Representative examples of the lesions for the three nonzero ratings are shown in the Figure. A rating of 1 involved minimal changes rarely mentioned in radiology reports because they are generally deemed to be of no significance for patients over 55 years of age. A rating of 2 was
defined as definite brain tissue changes of mild severity and of questionable significance. Moderate changes that were felt to be significant indicators of a possible disease process received a rating of 3. In this population there were no very severe HI. In some instances there were fewer than 10% of subjects in the grade 3 category (13 subjects had a 3 rating for subcortical gray matter HI; 4 subjects had a 3 rating for insular subcortex HI). These subjects were combined with those who had a rating of 2 into a mild/moderate category (Tables 3 and 4).

Data Analysis

We performed a series of ANOVAs of casual and ambulatory BPs and HR in a one-way group design (group = severity of lesion). Since both dependent and independent measures were influenced by age and sex, they were included as covariates in the analysis. Bartlett’s test showed that all of the variances in all analyses were homogeneous. When the overall F was significant \((P < 0.05)\), Tukey tests were used to determine between-group differences.

Results

Subject Characteristics

The sample consisted of 82 women and 62 men, aged 55 to 79 years, living in the community (Table 1). Racial composition was 112 Caucasians, 20 Asian Americans, 11 African Americans, and 2 Latinos. Only 5 subjects were current smokers. While the majority was retired, 36% were still employed. Subjects exercised about 10 hours per week and were highly educated, and almost half earned over $50,000 per year. Elevations in casual BP were restricted to 10% of the sample: 1 subject had stage 1 (mild) hypertension (154/94 mm Hg); 1 had stage 2 (moderate) hypertension (165/103 mm Hg); and 13 had isolated systolic hypertension (SBP 140 to 152 mm Hg, DBP 69 to 88 mm Hg). Among those with systolic hypertension, 7 subjects had SBP between 140 and 143 mm Hg. The remainder of the subjects were within the normotensive range. (For definitions of hypertension see Reference 14.)

White Matter HI

In general, the higher the severity rating of white matter HI the higher the level of BP during casual measurements as well as during awake and sleep periods (Table 2). This was particularly true for SBP, in which significant differences between moderate and either none or minimal ratings ranged from 7 to 14 mm Hg. Although DBPs tended to show similar differences, only the ambulatory DBP difference during

<table>
<thead>
<tr>
<th>TABLE 1. Characteristics of Sample</th>
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<tbody>
<tr>
<td>Age, y</td>
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<tr>
<td>M/F, n</td>
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<tr>
<td>Casual SBP/DBP, mm Hg</td>
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<tr>
<td>Body mass index, kg/m²</td>
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<tr>
<td>Exercise, h/wk</td>
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<tr>
<td>Education &gt;=4 y college, %</td>
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<tr>
<td>Income &gt;=$50,000, %</td>
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</table>

Values are mean (SD) unless otherwise indicated.
awake periods was significant. Also, subjects with the highest ratings had consistently higher BP variability during awake and asleep periods than subjects in the other rating categories, but significance was found only for SBP variability during awake periods. Greater severity was also associated with a smaller percentage drop in SBP and DBP from awake to asleep. HR was not significant.

Subcortical Gray Matter HI
Although all BP levels went up with increasingly higher ratings, only SBP was significant (casual measurements and ambulatory recordings while awake and asleep; Table 3). Differences between the two extreme groups (none and mild/moderate) varied between 6 and 10 mm Hg. DBP effects were not significant. In addition, the nocturnal HR decrease was less in the group with the greatest severity. None of the variability measures were significant.

Insular Subcortex HI
Both SBP and DBP (casual, awake, and asleep) had highly significant findings with regard to HI of the insular subcortex (the greater the rating the higher the BP) (Table 4). In comparisons of the extreme ratings (none versus mild/moderate), SBP differences ranged from 8 to 13 mm Hg and DBP differences from 5 to 7 mm Hg. While BP variability tended to increase with greater lesion severity, only HR variability during sleep was significant. The fall in HR from being awake to asleep was less in those subjects with the highest severity.

Influence of Other Variables
Subsequent models were developed in which we considered the impact of body mass index, anxiety, depression, and education on the analyses, but they did not affect any of the findings. Analyses of activity data during awake and asleep periods indicated that awakening and rising during the night had no appreciable effect on any of the ambulatory BP values. Using the actigraph method of ruling out sleep readings classified as “awake” reduced the number of readings used in calculations of BP and HR by 10% but had very little effect on the mean values. Use of information on subjective ratings of quality of sleep, number of hours slept, and number of

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TABLE 2. Casual and Ambulatory BP and HR Differences for Ratings of White Matter HI

<table>
<thead>
<tr>
<th></th>
<th>None (n=27)</th>
<th>Minimal (n=38)</th>
<th>Mild (n=53)</th>
<th>Moderate (n=26)</th>
<th>F (1/138)</th>
<th>P</th>
</tr>
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<tr>
<td>SBP</td>
<td>118.3 (14.8)</td>
<td>114.0 (12.6)</td>
<td></td>
<td>121.1 (14.1)</td>
<td></td>
<td>127.7 (12.4)</td>
</tr>
<tr>
<td>DBP</td>
<td>72.7 (11.0)</td>
<td>69.9 (8.4)</td>
<td>72.7 (8.1)</td>
<td>75.6 (7.3)</td>
<td>2.47</td>
<td>.065</td>
</tr>
<tr>
<td>HR</td>
<td>73.0 (10.2)</td>
<td>68.9 (7.8)</td>
<td>67.7 (8.7)</td>
<td>68.7 (8.5)</td>
<td>2.19</td>
<td>.092</td>
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<tr>
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<tr>
<td>SBP</td>
<td>125.7 (11.4)</td>
<td>122.2 (9.7)</td>
<td></td>
<td>126.6 (12.4)</td>
<td></td>
<td>132.5 (11.3)</td>
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<tr>
<td>DBP</td>
<td>74.8 (8.1)</td>
<td>71.7 (5.5)</td>
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<td>73.7 (6.6)</td>
<td></td>
<td>76.6 (5.5)</td>
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<tr>
<td>HR</td>
<td>76.5 (8.9)</td>
<td>73.4 (8.8)</td>
<td>71.5 (7.9)</td>
<td>72.3 (9.1)</td>
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<td>110.8 (13.3)</td>
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<td>115.0 (15.3)</td>
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<td></td>
<td>61.8 (7.4)</td>
<td></td>
<td>65.2 (8.2)</td>
</tr>
<tr>
<td>HR</td>
<td>64.6 (8.4)</td>
<td>61.6 (6.5)</td>
<td>61.4 (8.1)</td>
<td>63.2 (8.4)</td>
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<td><strong>Awake SD</strong></td>
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<tr>
<td>SBP</td>
<td>13.9 (2.8)</td>
<td>12.8 (2.6)</td>
<td></td>
<td>13.9 (2.7)</td>
<td></td>
<td>15.1 (3.6)</td>
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<tr>
<td>DBP</td>
<td>10.8 (2.8)</td>
<td>10.4 (3.1)</td>
<td>10.7 (2.8)</td>
<td>11.2 (3.1)</td>
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<td>.755</td>
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<tr>
<td>HR</td>
<td>10.4 (3.0)</td>
<td>10.1 (2.9)</td>
<td>10.3 (2.9)</td>
<td>10.3 (3.6)</td>
<td>0.16</td>
<td>.922</td>
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<tr>
<td><strong>Sleep SD</strong></td>
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<td></td>
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<tr>
<td>SBP</td>
<td>8.6 (2.6)</td>
<td>9.2 (2.9)</td>
<td></td>
<td>9.9 (3.2)</td>
<td></td>
<td>10.5 (3.4)</td>
</tr>
<tr>
<td>DBP</td>
<td>7.3 (2.3)</td>
<td>7.3 (2.1)</td>
<td>7.5 (2.7)</td>
<td>7.9 (2.9)</td>
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<td>.791</td>
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<td>HR</td>
<td>5.5 (2.2)</td>
<td>5.0 (2.1)</td>
<td>4.8 (3.0)</td>
<td>5.2 (2.0)</td>
<td>0.51</td>
<td>.679</td>
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<tr>
<td><strong>Percent fall</strong></td>
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<tr>
<td>SBP</td>
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<td>11.2 (4.9)</td>
<td></td>
<td>12.5 (5.6)</td>
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<td>13.2 (7.8)</td>
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<tr>
<td>DBP</td>
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<td>13.2 (6.5)</td>
<td></td>
<td>16.1 (7.1)</td>
<td></td>
<td>14.8 (9.0)</td>
</tr>
<tr>
<td>HR</td>
<td>15.5 (6.3)</td>
<td>15.6 (7.3)</td>
<td>14.0 (6.8)</td>
<td>12.4 (8.0)</td>
<td>1.32</td>
<td>.269</td>
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</tbody>
</table>

Values are mean (SD), adjusted for age and sex. SBP and DBP are given in mm Hg and HR in bpm. F and P values refer to one-way ANOVA; group differences are based on Tukey tests.

* P < .01 for difference between none and minimal.
† P < .05 for difference between none and mild.
‡ P < .05 for difference between none and moderate.
§ P < .05 for difference between minimal and moderate.
|| P < .1 for difference between minimal and moderate.
awakenings as covariates in analyses did not affect any of the analyses. Also, no subjects scored within the range of sleepiness encountered in patients with moderate or severe sleep apnea, nor were BP variables related to performance on the Epworth Scale.

Discussion
Despite the large numbers of statistical tests, most tests showed a consistent relationship between BP level and clinical ratings of severity of MRI T2 HI. In general, the more severe the rating the higher the BP (see Tables 2 through 4). Although other investigators have found similar results with white matter lesions in hypertensive patients, this is the first time that such a relationship has been reported in a large sample of elderly people with such low BPs. The casual mean BP for the group (120/72 mm Hg) contrasts sharply with that of the general population mean of individuals between the ages of 55 and 74 years (140/83 mm Hg). Although a diagnosis of hypertension had never been made in any of the subjects, their current pressures would lead to a diagnosis of stage 2 hypertension in 1, stage 1 hypertension in 1, and isolated systolic hypertension in the remaining 13. In the subjects with systolic hypertension, SBP was relatively low for this age group (140 to 152 mm Hg). It is interesting to note that the 1 subject with stage 2 hypertension had ratings of mild for subcortical gray matter and insular subcortex HI but had no white matter HI. Although we did not initially select individuals with such low BP, the sample resulted from the stringent exclusion criteria used in obtaining this group of healthy elderly men and women. Apparently a primary component of good health as one ages is the maintenance of a low BP.

DeCarli et al looked at white matter lesions in 51 nonhypertensive subjects with low casual BPs (124/78 mm Hg), but this sample consisted of young and elderly subjects with a much greater age range (19 to 91 years) than our sample. Their results indicated that both age and SBP were predictive of white matter HI volume. Other than being associated with age and hypertension, the significance of white matter changes in individuals without neurological problems is not completely understood. Since white matter changes are frequently detected in individuals over 60 years of age and are considered part of the aging process, their significance has been questioned. However, in a recent review Pantoni and Garcia concluded that subjects with HI were at increased risk of cerebrovascular events and deficits in some cognitive functions. Longitudinal studies of healthy populations would contribute to an under-

<table>
<thead>
<tr>
<th>TABLE 3. Casual and Ambulatory BP and HR Differences for Ratings of Subcortical Gray Matter HI</th>
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<tbody>
<tr>
<td>None (n=72)</td>
</tr>
<tr>
<td><strong>Casual</strong></td>
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<tr>
<td>SBP</td>
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<tr>
<td>DBP</td>
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<tr>
<td>HR</td>
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<td><strong>Awake</strong></td>
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<td>SBP</td>
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<tr>
<td>DBP</td>
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<tr>
<td>HR</td>
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<td><strong>Sleep</strong></td>
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<td>SBP</td>
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<td>DBP</td>
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<td>HR</td>
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<tr>
<td><strong>Awake SD</strong></td>
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<td>SBP</td>
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<td>DBP</td>
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<td>HR</td>
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<td><strong>Sleep SD</strong></td>
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<td>DBP</td>
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<td>HR</td>
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<tr>
<td><strong>Percent fall</strong></td>
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<tr>
<td>SBP</td>
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<td>DBP</td>
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<td>HR</td>
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</tbody>
</table>

Values are mean (SD), adjusted for age and sex. SBP and DBP are given in mm Hg and HR in bpm. F and P values refer to one-way ANOVA; group differences are based on Tukey tests.

*P<.05 for difference between none and mild/moderate.
†P<.01 for difference between none and mild/moderate.
standing of the significance of HI. Also, the association between BP and white matter lesions is more likely to be found for SBP than for DBP. The Copenhagen City Heart Study indicated that casual SBP was a stronger predictor of stroke than DBP. Our results confirm the relationship between casual SBP and white matter HI (Table 2). However, casual DBP followed a similar (although nonsignificant) trend in that subjects with greater lesion severity had higher BPs.

In addition to showing casual BP differences, our analyses of T2 HI indicated that subjects with varying severity ratings exhibited differences in ambulatory BPs. In general, the higher the severity rating for white matter HI the higher the awake and asleep SBP and DBP (Table 2). As with the casual BP, the greatest and most highly significant differences for ambulatory measures were found for SBP. The fact that BP remained relatively high during sleep indicates that BP elevations were fairly consistent throughout the day. Moreover, subjects with highest lesion severity were more likely than the other subjects to exhibit smaller decreases in nocturnal SBP and DBP and to have the greatest SBP variability while they were awake. Investigators found that elderly subjects with multilacunar lesions and higher grades of cerebrovascular damage (many with hypertension) had higher office and ambulatory BPs, particularly during sleep, and a smaller fall in BP during sleep than those with fewer cerebrovascular symptoms. Particularly among hypertensive patients, there was a higher prevalence of cardiovascular complications in individuals whose BPs failed to fall at night compared with those who showed decreased nocturnal BPs. The maintenance of a “continuous pressure overload” may contribute to the progression of left ventricular hypertrophy.

As SBP increased, ratings for subcortical gray matter HI indicated greater severity, although only the two extreme ratings (mild/moderate versus none) were significantly dif-

| TABLE 4. Casual and Ambulatory BP and HR Differences for Ratings of Insular Subcortex HI |
|----------------------------------|----------------|----------------|----------------|--------|--------|
| None (n=37) | Minimal (n=55) | Mild/Moderate (n=52) | F 1/139 | P |
| Casual | | | | |
| SBP | 114.9 (12.6)‡§ | 122.5 (13.1)† | 128.5 (15.2)§ | 11.92 | .0001 |
| DBP | 70.0 (8.4)§ | 73.4 (8.3) | 77.0 (8.8)§ | 8.30 | .0001 |
| HR | 68.9 (8.5) | 70.9 (8.7) | 67.4 (9.9) | 1.40 | .250 |
| Awake | | | | |
| SBP | 123.3 (10.5)§ | 127.7 (12.2) | 131.6 (12.1)§ | 5.92 | .003 |
| DBP | 72.3 (6.0)§ | 74.4 (6.3) | 77.3 (7.4)§ | 6.74 | .002 |
| HR | 73.7 (9.2) | 73.1 (7.9) | 71.4 (8.7) | 0.82 | .443 |
| Sleep | | | | |
| SBP | 106.7 (10.6)§ | 110.0 (13.4)¶ | 117.2 (14.8)§§ | 7.65 | .001 |
| DBP | 60.5 (5.8)§ | 61.8 (8.1)¶¶ | 66.5 (8.5)§§ | 7.70 | .001 |
| HR | 61.5 (7.7) | 63.6 (7.6) | 62.5 (8.7) | 0.94 | .392 |
| Awake SD | | | | |
| SBP | 13.5 (3.0) | 13.7 (2.8) | 14.9 (3.0) | 2.80 | .064 |
| DBP | 10.5 (3.0) | 10.6 (2.8) | 11.5 (2.9) | 1.42 | .245 |
| HR | 10.1 (2.9) | 10.5 (2.9) | 10.5 (3.6) | 0.20 | .822 |
| Sleep SD | | | | |
| SBP | 9.3 (2.8) | 9.6 (3.0) | 10.2 (4.0) | 0.97 | .380 |
| DBP | 7.5 (2.3) | 7.0 (2.4) | 8.0 (3.3) | 1.47 | .234 |
| HR | 4.9 (1.9)¶ | 4.6 (2.2)¶¶ | 6.2 (3.5)¶¶ | 4.28 | .016 |
| Percent fall | | | | |
| SBP | 13.4 (5.7) | 13.8 (6.4) | 10.9 (7.0) | 2.25 | .109 |
| DBP | 16.1 (6.4) | 16.8 (8.5) | 13.8 (9.3) | 1.46 | .236 |
| HR | 16.3 (5.0)*¶ | 12.7 (7.3)* | 12.3 (7.8)¶ | 5.30 | .006 |

Values are mean (SD), adjusted for age and sex. SBP and DBP are given in mm Hg and HR in bpm. F and P values refer to one-way ANOVA; group differences are based on Tukey tests.

*P<.05 for difference between none and minimal.
†P<.01 for difference between none and minimal.
‡P<.05 for difference between none and mild/moderate.
§P<.01 for difference between none and mild/moderate.
¶P<.05 for difference between minimal and mild/moderate.
different from each other (Table 3). Not only did subjects with HI have higher casual SBPs than those with ratings of none but SBP was higher during both awake and sleeping hours. The only other significant variable was percent fall in HR, indicating that the mild/moderate group had a smaller nocturnal HR fall. Howard et al. found that in a group of 35 community-dwelling elderly subjects, subcortical gray matter HI were associated with increases in SBP and DBP. Furthermore, hypertension has been found to be a risk factor for lobar and basal ganglia primary cerebral hemorrhage. In their relationship to the insular subcortex, cardiovascular factors displayed a somewhat different pattern. Here both SBP and DBP (casual, awake, and asleep) showed fairly large and highly significant differences between subjects with mild to moderate rating and those with ratings of none. Subjects with higher ratings had greater HR variability during sleep and a smaller nocturnal HR fall than those with no insular subcortex HI. These results agree with findings that the insular cortex has numerous interconnections with the limbic system, hypothalamus, and other areas of autonomic control. Patients with infarction of the insular cortex have been shown to have higher norepinephrine levels and a decreased or abolished fall in nocturnal BPs. There is evidence that the insular cortex mediates cardiovascular changes and that there may be a pathway within the lateral hypothalamic area linking the insular cortex with the heart.

The interpretation of these findings should be made in the context of the specific population sampled. This was a relatively homogeneous group of healthy, highly educated people who were primarily nonsmokers and who exercised frequently. No major health disorders had been diagnosed in the group nor had cases of hypertension been previously diagnosed. All medical test results were within the normal range. Even in these subjects, however, elevations in BP (primarily within the normotensive range) were associated with increased severity of T2 HI. In general, the higher the severity rating the greater the casual BPs (particularly SBP). In addition, further information was obtained by recording 24-hour ambulatory BP and HR. BP during awake and asleep periods, BP and HR variability, and nocturnal falls in BP and HR all showed relationships to T2 HI.

Of particular interest is the fact that BP and HR differences occurred not only between subjects with extreme HI ratings but also between those in the none and minimal categories. Although in only a few instances were these cardiovascular differences significant, there was a fairly consistent trend for BP to be higher in subjects with minimal severity of lesions of the subcortical gray matter and the insular subcortex when compared with subjects who had no HI at all. Apparently, small BP elevations can be associated with MRI changes in the elderly that are rarely of concern to radiologists. Moreover, the fact that elderly individuals with BPs at the upper normal ranges, and not just those with hypertension, may be at risk of brain damage has implications for modifications in lifestyle (ie, weight reduction, exercise, and dietary changes) in these men and women. Effective and early control of BP may do much to delay or even prevent onset of changes in the brain. It has been predicted that decreasing DBP by 2 mm Hg would lead to a 17% decrease in hypertension and a 15% drop in the risk of stroke and transient ischemic attacks. Moreover, recent findings showed that three quarters of all strokes occurred in subjects with SBPs of <144 mm Hg and DBPs of <95 mm Hg. More concern needs to be focused on subjects within the upper normotensive ranges of BP.

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Relationship Between Blood Pressure and Subcortical Lesions in Healthy Elderly People
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