Systolic Blood Pressure Tracking Over 25 to 30 Years and Cognitive Performance in Older Adults

Gary E. Swan, PhD; Dorit Carmelli, PhD; Asenath Larue, PhD

Objective—To determine the extent to which individual changes in systolic blood pressure (SBP) over a 30-year interval are associated with differential neuropsychological outcomes in old age.

Methods—Seven hundred seventeen survivors from the Western Collaborative Group Study, a longitudinal study of cardiovascular risk factors now in its 38th year of follow-up, with blood pressures measured in middle age (mean=45 years) and in old age (mean=75 years) and neuropsychological tests administered at follow-up were included in this analysis. Participants were grouped according to 30-year change in SBP (increased, decreased, or “normal”). Analyses focused on comparisons of neuropsychological performance of “high SBP trackers” (ie, those with persistent SBP≥140 mm Hg throughout adult life) and of SBP “decreasers” with the performance of those whose SBP was either stable or changed in an expected way over time.

Results—Only 7.5% of participants had elevated SBP in middle age, but 43.8% of participants had elevated SBP in old age. After adjustment for age, education, depression, clinically defined stroke, and use of antihypertensive medications and after exclusion of individuals with impaired cognitive performance at follow-up, high SBP trackers, 5.0% (n=36), performed consistently less well than the “normal” SBP subgroups on a composite measure of verbal learning and memory (P=0.04). When compared with the “normal” SBP subgroup, the SBP decreasers, 5.3% (n=38), performed less well on speeded performance (P=0.03).

Conclusions—There is a relatively small group of people who maintain elevated SBP throughout their adult lives. These persons are at increased risk for reduced verbal learning and memory function. There is also a group of individuals who experience a decrease in SBP and who are at risk for decreased psychomotor speed. Delineation of these 2 SBP subgroups may lead to further clarification of the effects of SBP on neurobehavioral function in older adults. (Stroke. 1998;29:2334-2340.)

Key Words: aging ■ blood pressure ■ cognition ■ neuropsychology

Elevated systolic blood pressure (SBP) is associated with reduced levels of cognitive performance and increased cognitive decline in the majority of investigations of this issue. Elevated baseline SBP levels and increased chronicity of hypertension were found to be associated with lower cognitive performance measured 12 to 14 years later for measurements taken when few, if any, participants were on antihypertensive medication. The long-term impact of elevated midlife SBP on reduced cognitive performance has been extended from the 14-year interval first reported by Elias et al to 25 years and to 30 years. The primary implication of these findings is that SBP in middle age that is elevated but not necessarily hypertensive may exert a measurable deleterious effect on the function of the brain over intervals as long as 3 decades. This could suggest the need for more aggressive management, beginning in middle age, of SBP in these individuals.

Although the long-term consequences of elevated midlife SBP for cognitive function now appear indisputable, 1 of the unanswered questions in this area is the extent to which individual differences in SBP tracking throughout adult life result in different neurobehavioral consequences. For example, the functional consequences of persistently elevated SBP over periods of as much as 30 years may be different from those associated with persistently low or moderate levels or those that occur as a result of gradually increasing SBP associated with aging. Under the assumption that the cumulative neurobehavioral consequences of SBP are more severe the longer the interval over which it is elevated, we hypothesized that the high SBP trackers would perform less well on neuropsychological tests taken at the end of the 25- to 30-year observation period than would any of the other tracking subgroups.
Subjects and Methods

Subjects

The Western Collaborative Group Study is a prospective cardiovascular epidemiological study that began in 1960–61 with 3152 healthy white men drawn from 10 large California corporations in the San Francisco Bay Area and Los Angeles.20–23 At intake, the age of the subjects ranged from 39 to 59, and all subjects were determined to be healthy and free of heart disease. Seven examinations occurred between 1960 and 1970 to monitor the incidence of cardiovascular disease in this cohort. During 1982 and 1983, the first long-term mortality follow-up of this cohort was conducted; from 1986 through 1988 and again from 1992 through 1994, subsequent follow-up examinations were conducted in a large subgroup of survivors of this cohort.

At the 1986 to 1988 follow-up (see Figure 1), 967 subjects (31% of the total cohort) were deceased. Five hundred seventy-three survivors of this cohort. Follow-up examinations were conducted in a large subgroup of survivors of this cohort.

At the 1992 to 1994 follow-up, an additional 363 (12% of the total cohort) were deceased. Four hundred twenty-one subjects (23% of all surviving subjects) participated by questionnaire only; 287 (16%) were unable or refused, and 381 subjects (21%) were lost to follow-up.25 A total of 1232 subjects participated in the examination, which included blood pressure (BP) measurements, anthropometric measures, and neuropsychological assessment. Extensive health histories were obtained by questionnaire and interview and later validated by review of medical records. Mean age of participants at this examination was 70.6 years (range, 60 to 86 years).

At the 1992 to 1994 follow-up, an additional 363 (12% of the total cohort) were deceased. Four hundred twenty-one subjects (23% of all surviving subjects) participated by questionnaire only; 287 (16%) were unable or refused, and 381 subjects (21%) were lost to follow-up. A total of 733 subjects participated in the examination, which included blood pressure (BP) measurements, anthropometric measures, and neuropsychological assessment. Extensive health histories were obtained by questionnaire and interview and later validated by review of medical records. Mean age of participants at this examination was 70.6 years (range, 60 to 86 years).

Risk Factor Assessment

In addition to age and neuropsychological status (see below), the following variables were assessed at the 1986 to 1988 and 1991 to 1993 exams. (1) Education: subjects indicated the amount of education they had acquired, on a 7-point scale (1 = less than 8th grade, 7 = doctoral level). (2) Stroke and transient ischemic attacks (TIAs) were determined by physician-validated self-reports. With the use of hospital records and physician reports, cerebrovascular diagnoses encompassing stroke and TIA were coded as International Classification of Diseases, 9th Revision (ICD-9) 430 to 438.9.25 (3) SBP and diastolic blood pressure (DBP; in millimeters of mercury) were measured by a trained technician according to published guidelines while the subject was in the seated position.26 (4) Antihypertensive medication status at follow-up was determined through coding of current medications as determined by physical inspection at the time of examination. The recorded BP medication was then categorized into therapeutic categories as either β-blocker, angiotensin-converting enzyme (ACE) inhibitor, calcium channel blocker, or diuretic. (5) Cardiovascular disease (CVD): This variable encompassed review of electrocardiograms and physician validation of self-reports of ischemic heart disease and myocardial infarction. With the use of hospital records, physician reports, and an ECG, we assigned cardiovascular diagnoses (ICD-9 codes 410 to 414, 427.5, and 428)25 according to published criteria. Information was reviewed by 2 physicians without knowledge of the participant’s cognitive status. (6) Depression: A score of greater than 5 on the Geriatric Depression Scale was the definition of probable depression. Total scores on this scale can range up to 15. (7) Body mass index (BMI) was determined from measured height (in meters) and weight (in kilograms) and calculated as kilograms per meters squared. (8) Diabetes was determined by physician-validated self-report. With the use of subsequent hospital and physician records, the diagnosis of diabetes was coded as ICD-9 250 to 250.9.25

Neuropsychological Measures

The follow-up examination of the surviving subjects also included the following neuropsychological tests. (1) The Iowa Screening Battery for Mental Decline29,30. This battery is composed of 3 tests assessing orientation to time, visuospatial skills and visual memory, and word-list generation (associative word fluency). (2) Mini-Mental State Examination: This 30-point test includes questions on orientation to time and place, registration, attention, calculations, recall, language, and visual construction. Scores of less than 23 have been used previously to indicate significant cognitive impairment.32 (3) Wechsler Adult Intelligence Scale–Revised Digit Symbol Substitution: This task required the subject to copy, over a 90-second period, a series of letter-like symbols paired with specific numbers. Adequate performance entails several cognitive and perceptual functions, including attention, visual perceptual and visuoconstructive abilities, sequencing, and short-term memory. (4) Color Trail Making Test: Like the traditional Trail Making Test, Color Trails is a brief psychomotor speeded task presented in 2 trials (hereafter referred to as Trails 1 and 2). The test measures sustained visual attention, visual scanning, and graphomotor skills in adults. Both trails entail drawing a line to connect in correct numerical sequence numbers scattered across a page; some numbers are circled in yellow and others in pink. In Color Trails 2, consecutive numbers of alternating color must be selected, and alternative color options must be ignored. All participants were assessed for color blindness before administration. Those reporting difficulty with color perception were not given the Color Trails or the Color-Word Interference Test. (5) Color-Word Interference Test: This test provides an index of a person’s ability to inhibit an overlearned response. Three stimulus cards are presented for which the subject must read printed color words, then identify color patches, and then name the color of ink for...
words that have been printed in conflicting colors (eg, the word “red” printed in green ink). (6) California Verbal Learning Test (CVLT). The CVLT is a test of multi-trial verbal free recall. A meta-analysis of the literature\(^4\) found the CVLT to be among the most sensitive of all tests for cognitive deficits associated with abnormal aging. Test responses were scored with personal computer–based software.\(^4\)

### Statistical Methods

Midlife SBP was defined as the mean of 7 SBP measurements taken over the span of 1960–61 through 1969–70. Each of the 7 measurements was itself a mean of 3 SBP measurements taken 5 minutes apart. Late-life SBP was defined as the mean of 2 SBP measurements taken during the follow-up exams from 1986 through 1998 (mean age=71 years) and from 1992 through 1994 (mean age=75 years). Each of the 2 SBP measures was itself a mean of 2 SBP measurements taken 5 minutes apart.

All the available BP measurements taken between 1960 and 1970 were used to calculate an overall mean of midlife BP. Subjects participating in fewer than 3 of the 7 annual exams between 1960 and 1970 were excluded. Subjects participating in 1 or both of the follow-up exams were included in the calculation of late-life BP.

The following categories of SBP level were created for this analysis: low (<120 mm Hg), medium (120 to 139 mm Hg), and high (≥140 mm Hg). An individual was considered to be “normal” if his SBP was consistently low or medium at both midlife and at follow-up or if his SBP increased over follow-up (eg, those whose SBPs increased from the low to the medium or high category or from the medium to the high category). If his SBP was consistently high at midlife and at follow-up, he was categorized as a “high tracker.” Those whose SBPs decreased (eg, those whose SBPs decreased from the high to the medium or low BP category or from the medium to the low category) were classified as “SBP decreasers.”\(^4\)

Univariate comparisons of participant characteristics in the different SBP tracking subgroups were evaluated using χ² tests for categorical response variables and ANOVA tests for continuous response variables.\(^4\) The analytical sample included 717 individuals with complete BP data from the 1960s, either of the 2 long-term follow-up exams, and neurobehavioral data from the 1992 through 1994 follow-up. The distribution of individuals within the 3 tracking subgroups without neurobehavioral data in the period 1992 to 1994, \(χ^2(2)=0.76, P=0.69\).

We conducted a principal components analysis (PCA) followed by a varimax rotation,\(^4\) to reduce complexity and redundancy among the cognitive measures used in this study. The minimum eigenvalue for retention of a component was set to ≥1.\(^4\) PCA identified 3 orthogonal components (eigenvalues were 5.9, 2.5, and 1.0, respectively) accounting for a total of 67.1% of the total intermeasure covariance. After rotation, the first factor, accounting for 32% of total covariance, was marked by very high correlations with measures of verbal memory (List A total, short- and long-delay cued and free recall from the CVLT). Factor loadings ranged from 0.93 for long-delay free recall to 0.86 for List A total learning. Loadings on the first factor for the other cognitive measures were low and ranged from 0.04 (Trails A) to 0.23 (Color-Word Interference). This factor was labeled “verbal memory.”

The second rotated factor, accounting for 26.4% of total covariance, was marked by high correlations with the tests of speeded performance (Trail Making A and B, Color Trail Making 1 and 2, Color-Word Interference, and Digit Symbol Substitution). Factor loadings for these variables ranged from a high of 0.71 for Trails B to 0.51 for Color Word Interference performance. Loadings for the remaining cognitive measures were moderate to low, ranging from −0.11 for short-delay cued verbal recall to −0.13 for verbal fluency. This factor was labeled “psychomotor speed.”

The third rotated factor, accounting for 9% of the total variance, was marked by a very high correlation with verbal fluency (\(r=0.81\)) and small to moderate correlations with the other tests of neurobehavioral function. Accordingly, this factor was labeled as “verbal fluency.”

Eigenvalues for the remaining 11 principal components identified in the initial PCA fell below the conventional cutoff of 1.0 and ranged from 0.90 to 0.09. The proportion of variance accounted for by each individual component was small and ranged from 6% to 1%.

Standardized scoring coefficients from each of the 3 factors were then used to generate 3 composite standardized scores (mean=0, SD=1) for verbal memory, speeded performance, and verbal fluency, for each subject included in this analysis. After the exclusion of 7 persons who scored below 23 on the Mini-Mental State Examination, the tracking subgroups’ 3 composite scores were then compared, using the general linear model to adjust for the effects of age, education, depression, clinically defined stroke, and the use of antihypertensive medications.

### Results

#### Distribution of SBP in Midlife and Late-Life

Table 1 shows the joint distribution of SBP categories in the 717 participants with both midlife and late-life measurements. In midlife, only 7.5% of this group of survivors had SBP in the high category. The percentage of individuals with elevated SBP in late-life was 43.8%. Overall, 31.8% “tracked,” ie, remained stable throughout the period of follow-up with respect to their SBP level. Ten percent of participants were low SBP trackers, and 5% were high SBP trackers. Sixty-three percent of the sample showed an increase in SBP over the follow-up, and 5.3% showed a decrease in SBP over the follow-up.

#### Characteristics of Tracking Subgroups

Table 2 presents characteristics of the 3 SBP tracking subgroups defined for this analysis. There were no significant differences between the tracking subgroups with respect to age, \(F_{(2,714)}=1.72, P=0.18\); education, \(F_{(2,714)}=2.27, P=0.10\); or BMI, \(F_{(2,681)}=0.28, P=0.76\). There were also no significant
associations observed between tracking subgroup membership and prevalence of stroke, \( \chi^2 = 3.27, P = 0.20 \); TIA, \( \chi^2 = 1.95, P = 0.38 \); or coronary heart disease, \( \chi^2 = 4.60, P = 0.10 \).

As expected, significant group differences were observed between midlife (1960 through 1970) SBP, \( F(2,714) = 234.56, P = 0.0001 \), follow-up SBP in 1988, \( F(2,611) = 20.12, P = 0.0001 \), and follow-up SBP in 1992, \( F(2,706) = 34.48, P = 0.0001 \); all pair-wise comparisons were considered significant at \( P \leq 0.05 \). Persons in the normal SBP trajectory subgroup experienced an average increase of 24 mm Hg (a 20.1% increase in SBP over the life span), whereas those in the high tracking subgroup increased an average of 16.6 mm Hg (an 11.2% increase over the follow-up interval). An average decrease of 9.1 mm Hg (a change of -6.7%) was observed in persons experiencing a reduction in SBP over the follow-up interval.

Compared with those with normal SBP over the follow-up, high SBP trackers had a higher frequency of diabetes, \( \chi^2 = 9.75, P = 0.008 \); were more likely to be using antihypertensive medication in 1988, \( \chi^2 = 14.12, P = 0.001 \); and to be use antihypertensive medication at the 1988 and 1992 follow-ups. SBP decreasers who were using BP medication were more likely to be using \( \beta \)-blockers, \( \chi^2 = 13.52, P = 0.001 \).

Neuropsychological Performance of Tracking Subgroups

Figure 2 presents mean scores and associated standard errors for each of the tracking subgroups after adjustment for potential confounders and the exclusion of cognitively im-

**TABLE 2. Subject Characteristics in Relation to Long-Term Changes in SBP (n=717)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normals (n=553–643)</th>
<th>High-High (n=30–36)</th>
<th>Decreased (n=31–38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y†</td>
<td>75.7* (4.2)</td>
<td>76.4* (3.4)</td>
<td>76.8* (4.8)</td>
</tr>
<tr>
<td>Education, level†</td>
<td>4.5 (1.2)</td>
<td>4.1* (1.2)</td>
<td>4.4* (1.2)</td>
</tr>
<tr>
<td>BMI, kg/m²†</td>
<td>26.5* (3.3)</td>
<td>26.9* (3.2)</td>
<td>26.8* (3.9)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP/DBP, 1960–1970</td>
<td>119.6±77.3* (8.4/5.8)</td>
<td>147.6±91.6* (6.9/5.6)</td>
<td>135.4±86.5* (11.2/6.4)</td>
</tr>
<tr>
<td>SBP/DBP, 1988</td>
<td>131.4±74.8*± (17.6/6.9)</td>
<td>147.3±78.4* (18.8/12.3)</td>
<td>119.1±70.7* (14.1/8.1)</td>
</tr>
<tr>
<td>SBP/DBP, 1992</td>
<td>143.6±75.6* (20.1/11.0)</td>
<td>164.2±79.2* (14.8/11.5)</td>
<td>126.3±70.4* (16.1/9.6)</td>
</tr>
<tr>
<td>GDS&gt;5, %†</td>
<td>5.7</td>
<td>2.8</td>
<td>16.2*</td>
</tr>
<tr>
<td>Stroke, %†</td>
<td>6.7</td>
<td>13.9</td>
<td>10.5</td>
</tr>
<tr>
<td>TIA, %†</td>
<td>2.0</td>
<td>5.6</td>
<td>2.6</td>
</tr>
<tr>
<td>CHD, %†</td>
<td>28.5</td>
<td>30.6</td>
<td>44.7</td>
</tr>
<tr>
<td>Diabetes, %†</td>
<td>9.2</td>
<td>25.0</td>
<td>7.9*</td>
</tr>
<tr>
<td>MMSE&lt;23, %†</td>
<td>1.7</td>
<td>5.6</td>
<td>10.8*</td>
</tr>
</tbody>
</table>

Antihypertensive medications, %

<table>
<thead>
<tr>
<th>Type, %†</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>16.0</td>
<td>55.6</td>
<td>29.7*</td>
</tr>
<tr>
<td>( \beta )-blocker</td>
<td>13.1</td>
<td>25.0</td>
<td>32.4*</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>13.3</td>
<td>16.7</td>
<td>18.9</td>
</tr>
<tr>
<td>1992</td>
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<td>13.3</td>
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<td>18.9</td>
</tr>
</tbody>
</table>

GDS indicates Geriatric Depression Scale; CHD, coronary heart disease; and MMSE, Mini-Mental Status Examination. Values are mean (SD), or % as indicated. Means with different letters are significantly different at an overall \( \alpha = 0.05 \) significance level.

*Significant \( \chi^2 \) association at \( P \leq 0.05 \).

†Denotes a measurement taken at follow-up.

As expected, significant group differences were observed between midlife (1960 through 1970) SBP, \( F(2,714) = 234.56, P = 0.0001 \), follow-up SBP in 1988, \( F(2,611) = 20.12, P = 0.0001 \), and follow-up SBP in 1992, \( F(2,706) = 34.48, P = 0.0001 \); all pair-wise comparisons were considered significant at \( P \leq 0.05 \). Persons in the normal SBP trajectory subgroup experienced an average increase of 24 mm Hg (a 20.1% increase in SBP over the life span), whereas those in the high tracking subgroup increased an average of 16.6 mm Hg (an 11.2% increase over the follow-up interval). An average decrease of 9.1 mm Hg (a change of -6.7%) was observed in persons experiencing a reduction in SBP over the follow-up interval.

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**Neuropsychological Performance of Tracking Subgroups**

Figure 2 presents mean scores and associated standard errors for each of the tracking subgroups after adjustment for potential confounders and the exclusion of cognitively im-

![Figure 2](http://stroke.ahajournals.org/)

**Figure 2.** Mean scores (bars indicate SEM) on the verbal memory, psychomotor speed, and verbal fluency factors for the BP tracking subgroups in the Western Collaborative Group Study.
paired individuals. High SBP trackers performed significantly less well on verbal memory ($M = -0.29 \pm 0.18$) than did those classified as having a normal blood pressure trajectory ($M = 0.03 \pm 0.04$), $P = 0.039$, 1-tailed test. High SBP trackers had lower scores on the memory factor score than those whose SBP decreased over the follow-up ($M = -0.03 \pm 0.18$), although this difference did not reach significance.

In addition, SBP decreasers performed significantly less well on speeded performance ($M = -0.29 \pm 0.17$) than did those exhibiting a normal SBP trajectory ($M = 0.03 \pm 0.04$), $P = 0.03$, 1-tailed test. High SBP trackers appeared to perform better than the SBP decreasers on speeded performance ($M = -0.05 \pm 0.18$), but, again, this difference did not reach significance.

No significant differences were observed in the adjusted verbal fluency factor score across the 3 SBP tracking groups.

**Discussion**

The relatively few longitudinal studies of SBP tracking from middle to older age suggest that individual differences in SBP tracking continue throughout the life span$^{44-47}$ and that adult high SBP trackers encounter increased risk for stroke and diabetes$^{44}$ and ischemic heart disease in late life.$^{46}$ Whereas DBP tends to drop with increasing age, SBP continues to increase with age regardless of the initial level in early to middle adulthood. The plateauing of mean arterial pressure along with the concomitant increase in pulse pressure have led some investigators to conclude that large-artery stiffness (as opposed to peripheral vascular resistance) is the primary contributor to the rise in SBP in old age.$^{47}$

Although the dynamic nature of BP is widely known in the literature on cardiovascular aging, it has rarely been taken into account in epidemiological investigations of the BP-cognition connection. The main findings from the present analysis are (1) despite the availability of BP medication, there remained a small group of persons (5% of the present sample) whose SBP was high in middle age and remained high when assessed again 25 to 30 years later, in late life; (2) these high tracking individuals appear to be at risk for reduced verbal learning and memory function when compared with other SBP subgroups; and (3) individuals whose SBP decreased over the life span (5.3% of the present sample) appear to be at risk for reduced psychomotor speed performance in old age.

The cumulative effect of high SBP tracking can be seen in the somewhat higher prevalence of stroke at follow-up in this subgroup relative to all other SBP tracking subgroups. It is interesting to note the very high prevalence of the use of antihypertensive medication in the group with consistently elevated SBP. This finding would suggest that despite the fact that the use of these medications may have been effective in reducing DBP to lower levels, their impact on SBP was less in magnitude.

Individuals whose SBPs declined over the follow-up interval of this study had a comparatively high prevalence of depression (16.2%) and coronary heart disease (44.7%), both of which are related to impaired cognitive function.$^{48}$ Low SBP in the elderly has previously been shown to be related to the prevalence of heart failure, limitations in activities of daily living, and cognitive impairment,$^{49}$ as well as to an increased risk of 5-year mortality.$^{50}$ Declining SBP may result from dementing illness,$^{51}$ cardiac insufficiency,$^{49}$ or a number of other disease conditions.$^{52}$

Although the high SBP trackers and the SBP decreasers both performed less well on 2 of 3 measures of neurobehavioral function than did the normal trajectory subgroup, they did not differ statistically with respect to their level of verbal memory and psychomotor speed performance. However, inspection of Figure 2 suggests a trend in which the high SBP trackers appear to be at greatest risk for decrements in verbal memory, and the SBP decreasers were most likely to show reduced psychomotor speed. This pattern suggests that the causal connection may well be reversed for the 2 groups. In the case of the high SBP trackers, the deleterious effects of the elevated SBP are focused specifically on memory functions. In the case of SBP decreasers, chronic disease and systemic decline may operate to influence declining SBP and psychomotor speed. In this context, we note that a previous investigation of ours reported a relationship between slower psychomotor speed and increased 5-year mortality.$^{53}$ Our previous finding, in concert with the finding that low BP is also a predictor of 5-year mortality in older adults,$^{50}$ suggests to us that 1 of the next steps for investigation of risk factors for mortality in older adults should be the inclusion of decline in cognitive function and SBP in the same predictive model. This approach would enable us to determine the relative importance and independence of these 2 processes vis-à-vis mortality.

Because of its epidemiologic nature, this study leaves open the question of potential mechanisms underlying the association between high SBP tracking and neurobehavioral function. Numerous possibilities exist including disturbed cerebral perfusion, with consequent negative impact on brain cell metabolism$^{15,16}$; cerebral infarction; and/or the presence of diffuse white matter lesions.$^{54}$ Even in mildly hypertensive subjects, regional cerebral blood flow is reduced in the frontal cortex and basal ganglia, compared with normotensive subjects. In moderate-to-severe hypertensives, cerebral oxygen metabolism is diminished, and there are higher prevalences of ventricular enlargement and white matter vascular lesions.$^{55-58}$ Recent studies involving the use of MRI have found an association between hypertension and brain atrophy,$^{59}$ leukoaraiosis,$^{60}$ lacunae and periventricular hyperintensities,$^{61-63}$ prevalence and severity of white matter hyperintensities,$^{64-68}$ and cognitive decline.$^{64}$ The presence of white matter hyperintensities in elderly adults free of disease has recently been shown to be related to elevated mean arterial pressures, as well as to poorer cognitive performance on tasks involving speed and complex mental processing.$^{69}$ Recent studies of large samples of older subjects also found an association between MRI findings and cognition.$^{56,57}$ These findings suggest that subclinical changes in brain morphology may underlie the previously observed associations between SBP and cognitive function.

In the present study, the high SBP trackers were more likely to be using ACE inhibitors, whereas the SBP decreasers were most likely to be using β-blockers. The relationship of various classes of BP medication to differential neurobe-
havioral outcomes is inconsistent across a variety of studies.\textsuperscript{21–7} Although small sample size precludes the stratification of the sample based on type of BP medication, it is important to note that we included the use or nonuse of BP medication as an adjustment variable in the predictive models of neurobehavioral function. In none of the 3 models did the BP medication variable exhibit a significant association with cognitive outcomes.

The strong points of the present study include its use of a relatively large number of BP measurements to estimate BP in middle and late life, the long duration of follow-up, and a comprehensive assessment of neurobehavioral function in late life. A limitation of the study is its use of data from male participants only. Females were not available to this analysis for no reason other than that the study’s inception (1960) occurred in an era when a lack of knowledge about gender differences in CVD risk factors led to the erroneous conclusion that males and females are similar in these respects. Because more recent findings suggest the presence of strong gender differences with respect to CVD risk factor profiles and the relationship of CVD to dementia, the results from the present analysis will need to be confirmed in older women. Another limitation of the present study concerns the substantial attrition experienced by this cohort over the duration of the 25- to 30-year follow-up. The data actually used for analysis are based on testing of 39% of the original cohort from the period 1986 to 1988 and on 34% of the cohort from 1992 to 1994. Although this is not uncommon for a study of this length, the effect of attrition because of premature death, disease, or disability is most likely to have resulted in an underestimation of the true predictive relationship seen here.

On the basis of these results, it does appear that there is a relatively small group of individuals whose SBP remains elevated over the life span despite the use of antihypertensive medication. Whether the neurobehavioral differences in these individuals are associated with an increased incidence of brain morphologic changes, such as “silent” stroke, brain atrophy, or white matter disease, remains to be determined.

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