Stress-Induced Blood Pressure Reactivity and Incident Stroke in Middle-Aged Men

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Background and Purpose—Exaggerated blood pressure reactivity to stress is associated with atherosclerosis and hypertension, which are known stroke risk factors, but its relation to stroke is unknown. Previous work also indicates that the association between reactivity and cardiovascular diseases may be influenced by socioeconomic status.

Methods—The impact of blood pressure reactivity and socioeconomic status on incident stroke was examined in 2303 men (mean age, 52.8 ± 5.1 years) from a population-based, longitudinal study of risk factors for ischemic heart disease in eastern Finland. Reactivity was calculated as the difference between blood pressure measured during the anticipatory phase of an exercise tolerance test (before exercise) and resting blood pressure, measured 1 week earlier. Mean systolic reactivity was 20 mm Hg (±15.9), and mean diastolic reactivity was 8.6 mm Hg (±8.5). Socioeconomic status was assessed as years of education. One hundred thirteen incident strokes (90 ischemic) occurred in 11.2 (±1.6) years of follow-up.

Results—Men with exaggerated systolic reactivity (≥20 mm Hg) had 72% greater risk of any stroke (relative hazard ratio [RH], 1.72; 95% CI, 1.17 to 2.54) and 87% greater risk of ischemic stroke (RH, 1.87; 95% CI, 1.20 to 2.89) relative to less reactive men. Moreover, men who were high reactors and poorly educated were nearly 3 times more likely to suffer a stroke than better educated, less reactive men (RH, 2.90; 95% CI, 1.66 to 5.08). Adjustment for stroke risk factors had little impact on these associations. Diastolic reactivity was unrelated to stroke risk.

Conclusions—Excessive sympathetic reactivity to stress may be etiologically important in stroke, especially ischemic strokes, and low socioeconomic status confers added risk. (Stroke. 2001;32:1263-1270.)

Key Words: ischemia ■ reactivity ■ social class ■ stress ■ stroke

Cardiovascular reactivity reflects underlying sympathetic nervous system activation and has been shown to vary according to individual characteristics (eg, personality factors, emotions), environmental exposures (eg, job stress, socioeconomic adversity), interpersonal and social contexts and interactions, and genetic predispositions to disease (eg, positive family history of hypertension or heart disease).1–5 Typically, this sympathetic hyperreactivity is manifest as excessive blood pressure (BP) or heart rate responses to psychological or behavioral stressors or stressful situations.5 Several human and animal studies support the hypothesis that exaggerated hemodynamic or cardiovascular reactivity to stress contributes to elevations in BP, carotid atherosclerosis, and coronary artery disease.6–13 Findings are not entirely consistent,14,15 however, with some evidence that the clinical significance of the association between reactivity and disease may be limited.16 Others have suggested that pathological consequences of reactivity may occur only in the presence of chronically stressful social environments.17

There are several recognized stroke risk factors, including hypertension, atherosclerosis, and atrial fibrillation. These risk factors are most strongly related to nonhemorrhagic stroke, and each involves arousal or activation of the autonomic nervous system, which suggests that sympathetic activation plays a role in stroke and particularly ischemic stroke. Thus, it stands to reason that stress-induced cardiovascular reactivity also may contribute to increased risk of stroke and especially stroke resulting from ischemia or ischemic mechanisms. To our knowledge, no prior population study has tested this hypothesis.

Stroke incidence and mortality are known to vary inversely with socioeconomic position.18–20 Similarly, as noted above,
stress-induced reactivity varies by environmental exposures and socioeconomic position, although the evidence linking stress-induced reactivity and socioeconomic position is mixed. Carroll and colleagues reported that systolic BP (SBP) reactions to a psychological task (Raven’s matrices) were positively related to occupational grade in a sample of British male civil servants, whereas Gump et al. found that BP reactivity to 2 α-adrenergic tasks (mirror tracing, cold pressor) was greater in children and adolescents from socioeconomically disadvantaged families (determined by the parents’ education and occupations). The nature of the tasks used in these 2 studies may account for the discrepancies in their results. Tasks that require greater psychological engagement in order to perform well, such as Raven’s matrices, which is a test of nonverbal intelligence, or computer-oriented tasks, which may be intimidating to those without computer experience, may elicit stronger cardiovascular reactions among those who become differentially engaged in the task. It is plausible that such engagement could vary by educational level. On the other hand, it has been hypothesized that the more adverse circumstances and chronic stress typically experienced by those in lower socioeconomic strata may contribute to exaggerated cardiovascular response to stress. We previously have reported that the effect of reactivity on progression of intimal-medial thickening (IMT) is potentiated in men of lower socioeconomic status (SES), which supports the hypothesis that the impact of reactivity on disease depends in part on one’s social environment and associated stressors. Thus, it may be that the relation of stress-induced reactivity to stroke also varies by SES.

The present study investigated the relation between stress-induced BP reactivity and subsequent 11-year risk of stroke in a population sample of >2300 middle-aged men. Using data from the Kuopio Ischemic Heart Disease (KIHD) Risk Factor Study, an ongoing study of biopsychosocial risk factors for cardiovascular disease, we were able to examine the independent effects of reactivity on stroke risk, after taking into consideration known risk factors for stroke. Secondly, we examined joint effects of reactivity and SES on stroke risk.

Subjects and Methods

Study Population

The KIHD Study is a comprehensive, population-based study of biological, socioeconomic, and psychosocial risk factors for atherosclerosis, heart disease, mortality, and other outcomes among middle-aged men from Kuopio, Finland, and surrounding rural communities in eastern Finland. Participants included 2682 men (82.9% of eligible), aged 42, 48, 54, or 60 years, who were enrolled between March 1984 and December 1989 (see details on the study protocol below). Subjects were excluded from the present analyses if they had a history of stroke (n=60), missing information on the measure of BP reactivity (n=255), or missing data on covariates (n=64), leaving a total of 2303 men eligible for the present study. The measurement protocol for assessing SBP and diastolic BP (DBP) included a 15-minute supine rest with BP measured 3 times at likely to be current smokers and to take medications for hypertension and hypercholesterolemia (P<0.03) but did not differ from participants in terms of resting BP, fibrinogen, body mass index (BMI), alcohol consumption, LDL or HDL cholesterol, or prevalence of diabetes at baseline. Baseline subject characteristics are shown in Table 1.

Study Protocol

The baseline study consisted of 2 examination days, separated by 1 week. Participants provided information on health habits, including diet, smoking, and alcohol consumption, family and personal history of disease, medications, SES, social support and social networks, and various psychological characteristics. Participants also underwent a medical examination, including measurement of height, weight, percent body fat, and BP (see details below), ultrasonographic assessment of carotid atherosclerosis, and a bicycle ergometer maximal exercise tolerance test. Lipids, hematicostatic factors, and plasma glucose and insulin, among other biochemical substrates, were determined from venous blood samples obtained on the first examination day, after overnight fasting and abstinence from smoking (12 hours), alcohol (3 days), and analgesics (7 days). Blood was drawn without tourniquet after a 30-minute supine rest, with the use of Terumo Venoject VT-100 FZ vacuum tubes, and cooled immediately on ice (4°C).

Complete details of the KIHD Study protocol and recruitment procedures have been reported previously. The KIHD Study was approved by the University of Kuopio Research Ethics Committee and conducted according to their established guidelines for human research participants and data confidentiality.

Measurement of BP and Reactivity

The measurement protocol for assessing SBP and diastolic BP (DBP) included a 15-minute supine rest with BP measured 3 times at

### TABLE 1. Mean Values or Prevalence of Baseline Subject Characteristics

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Value (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>2303</td>
<td>52.8 (5.1)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
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<td>26.8 (3.4)</td>
</tr>
<tr>
<td>V̇O₂max, mL/(kg · min)</td>
<td></td>
<td>30.9 (8.9)</td>
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<td>SBP, mm Hg</td>
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<td>DBP, mm Hg</td>
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<td>88.2 (10.8)</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td></td>
<td>4.0 (1.0)</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td></td>
<td>1.3 (0.3)</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td></td>
<td>3.0 (0.5)</td>
</tr>
<tr>
<td>Alcohol consumption, g/wk†</td>
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<tr>
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</tr>
<tr>
<td>≥6 years of school</td>
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<td>35.3%</td>
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<td>≥9 years of school</td>
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<td>35.4%</td>
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<tr>
<td>Smoking status</td>
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</tr>
<tr>
<td>Never</td>
<td></td>
<td>27.3%</td>
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<tr>
<td>Former</td>
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<td>39.5%</td>
</tr>
<tr>
<td>Current†</td>
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<td>33.2%</td>
</tr>
<tr>
<td>Diabetes</td>
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<tr>
<td>Medication use</td>
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<tr>
<td>Antihypertensive</td>
<td></td>
<td>20.4%</td>
</tr>
<tr>
<td>Cholesterol-lowering</td>
<td></td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Values in parentheses are SD.

*Excludes 291 nondrinkers; 1 drink has approximately 13 g of alcohol.
†Among current smokers, mean (SD) pack-years were 26.3 (18.7).
and modeled continuously. Use of medications for hypertension or hypercholesterolemia, confirmed during the medical examination, was modeled with dummy-coded variables. Prevalent diabetes, confirmed if a participant reported currently using diet or medication to control diabetes or if his fasting blood glucose level was $\geq 6.7$ mmol/L (120 mg/dL) was modeled with a dummy-coded variable. (Self-reported history of and/or use of medication for atrial fibrillation also was obtained at the baseline examination. However, only 10 participants had a history of atrial fibrillation, and none of these had a stroke during the follow-up. Consequently, we did not include a covariate representing this risk factor in our multivariate models.)

### Results

A total of 113 first strokes was identified during the 11 years of follow-up, with 90 of them determined to be ischemic or thrombotic, 21 determined to be hemorrhagic, and 2 undifferentiated. The average change in SBP in anticipation of exercise was 20 mm Hg (SD, 15.9; median, 19). The corresponding change in DBP was 8.6 mm Hg (SD, 8.5; median, 8). On average, participants reported 8.7 years (SD, 3.5) of education. Education was significantly, inversely related to both SBP ($b, -0.49; t, -5.18; P<0.0001$) and DBP changes ($b, -0.15; t, -3.04; P<0.003$) in anticipation of exercise.

### All Strokes

A Cox proportional hazards model, with covariates for age and resting SBP, found that each 1-mm increase in SBP in anticipation of exercise corresponded to a significant 1-point increase in risk of stroke (relative hazard ratio [RH], 1.01; 95% CI, 1.00 to 1.02). Dichotomizing respondents into high (greater than the median) and low reactors (equal to or less than the median) showed that men whose SBP rose $>19$ mm Hg in anticipation of exercise had a 72% greater risk of stroke over the subsequent 11 years than men who were less reactive ($P<0.006$) (Table 2). This association was modified only slightly and remained significant after adjustments for age, resting SBP, SES, smoking, alcohol consumption, BMI, $V_{\text{O}}_{2}\max$, LDL and HDL cholesterol, fibrinogen, history of diabetes, and use of medication for hypertension or hypercholesterolemia. Anticipatory diastolic response was not related to increased stroke risk.

### Reactivity and Stroke Risk by Type of Stroke

The majority (79.6%) of incident strokes that occurred in our population were due to ischemia or thromboembolism. Analyses that limited the outcome to these nonhemorrhagic strokes produced results similar to, albeit slightly stronger than, those seen for all strokes combined. Each 1-mm increase in the anticipatory SBP response corresponded to a significant 1.5% increased risk of ischemic stroke (RH, 1.015; 95% CI, 1.00 to 1.03), with adjustment for age and resting SBP. Modeling SBP reactivity categorically showed that high reactors had 87% greater risk relative to men who were less reactive in anticipation of exercise ($P<0.005$) (Table 2). Inclusion of covariates representing known stroke risk factors modified this association only slightly, with high reactors demonstrating a significant 74% excess risk of ischemic stroke in the fully adjusted model. DBP reactivity was unrelated to ischemic strokes.
Neither SBP reactivity nor DBP reactivity was significantly related to risk of hemorrhagic stroke. However, relatively few strokes in our population were due to hemorrhage, and it is therefore likely that we did not have adequate power to reliably assess these associations.

**SES, Reactivity, and Risk of Stroke**

Because stroke incidence and mortality are typically higher in lower SES groups and there is some evidence that cardiovascular reactivity varies inversely with SES, we also sought to determine the joint effects of SBP reactivity and SES on stroke risk. Education was significantly associated with stroke risk in the multivariate model reported in Table 2, with increasing education associated with decreasing risk (RH, 0.90; 95% CI, 0.83 to 0.97). Subsequent categorical analysis using approximate tertiles of education corresponding to primary school or less (=6 years of school), some vocational training or education beyond primary school but no high school (7 to 8 years of school), and some high school or more (≥9 years of school) showed that the least educated men were at increased risk of stroke (RH, 2.03; 95% CI, 1.22 to 3.37) relative to the best educated men, but those with 7 to 8 years of education were not (RH, 1.33; 95% CI, 0.79 to 2.23).

Consequently, to assess the joint effects of SBP reactivity and education on risk of stroke, we conducted a set of Cox proportional hazards models that included terms representing the main effects of reactivity and education as well as their interaction for all strokes combined and for ischemic strokes. Reactor status was dichotomized by a median split of SBP response in anticipation of exercise, as above, and education was dichotomized as primary school or less versus greater than primary school on the basis of the aforementioned findings for education. The interaction term was the cross product of these 2 terms.

We did not observe a significant, multiplicative interaction between reactor status and education for either all strokes combined (RH, 0.75; 95% CI, 0.35 to 1.60) or ischemic strokes (RH, 0.93; 95% CI, 0.39 to 2.20). However, we did find significant main effects for both reactor status and education (RH, 1.93; 95% CI, 1.15 to 3.26, and RH, 2.00; 95% CI, 1.09 to 3.67, respectively) with all strokes as the outcome. Moreover, contrasting men with both risk factors (high reactors with low education) with men with neither risk factor showed that reactive men with the least education had the greatest risk of stroke (RH, 2.90; 95% CI, 1.66 to 5.08) after adjustment for age and resting SBP. With ischemic strokes as the outcome, we observed a marginally significant main effect for education (RH, 1.76; 95% CI, 0.87 to 3.55) and a significant main effect for reactor status (RH, 1.90; 95% CI, 1.04 to 3.45) and again saw the greatest risk of stroke in men with both risk factors (RH, 3.11; 95% CI, 1.67 to 5.77) compared with men with neither risk factor. Risk factor adjustments produced only minor decrements in the point estimates and thus showed little effect of confounding by known stroke risk factors. For illustrative purposes, we have graphed the risk factor–adjusted results of the contrasts between the 4 groups that are identified by jointly considering reactor status and education (Figure). Although the interaction term between reactivity and education was not significant in our models, we believe that it is informative to note the combined main effects of reactor status and low education.

**Discussion**

This study provides convincing evidence that exaggerated BP responses to stress contribute to increased risk of stroke and particularly stroke due to ischemia or thromboembolism in middle-aged and older men. The association between reactivity and incident stroke was modified very little by known risk factors for stroke. These data support the growing literature on the importance of hemodynamic or cardiovascular reactivity in the development and progression of cardiovascular diseases. To our knowledge, this is the first study to link reactivity to excess risk of stroke.

We also found that men who had limited education were at greater risk of stroke than more educated men, which is consistent with prior research showing an inverse socioeconomic gradient for stroke incidence and mortality.
cardiovascular disease. Our study was not designed to test activity also may be conceptualized as a mediating mechanism of stroke over the intervening 11 years of follow-up. Reac-
tion was inversely related to reactivity in this study. Moreover, analysis of the joint effects of low SES and reactivity on risk of stroke showed that, while there was not a differential effect of reactivity among the poorly educated men (i.e., we did not observe a significant statistical interaction between reactivity and education on stroke risk), men with both risk factors in our study were nearly 3 times more likely to have had a stroke during the follow-up period compared with men who had neither risk factor. These results suggest that low SES adds to the risk of stroke associated with stress-induced autonomic arousal. However, as noted and as shown in the Figure, both SES and reactivity uniquely contributed to exceed stroke risk.

In this study stress-induced reactivity was conceptualized and modeled as a characteristic of the individual. Indeed, we found that the most reactive participants had the greatest risk of stroke over the intervening 11 years of follow-up. Reactivity also may be conceptualized as a mediating mechanism by which psychological or social factors increase risk of cardiovascular disease. Our study was not designed to test this model. The fact that we found additive but not interactive effects in our analyses in which we modeled the joint effects of reactivity and low SES suggests that the characteristic of reactivity has significant, independent health effects. Moreover, demonstrating that stress-induced reactivity increases stroke risk is an important prerequisite to future studies that may seek to examine whether such reactivity mediates the relation between various psychosocial characteristics and stroke.

The inverse association between reactivity and SES observed here is consistent with the findings reported by Gump et al but in contrast to results reported by Carroll et al.

Variations in our respective findings may very well relate to the types of tasks used, which differ in all 3 studies. For example, we have previously argued that the anticipatory period before exercise, the stressor used in the present study, can be characterized as a period of psychophysiological arousal attendant to an impending challenge and thus represents a measure of stress-induced reactivity. Differences between this reactivity measure and the type of cognitive task used in the study of Carroll et al may account for the discrepancies in our findings. It may be that tasks not dependent on scholastic achievement, in contrast to any number of verbal or nonverbal IQ tests, may yield more consistent results across studies. Additionally, as noted earlier, it is speculated that psychological engagement that influences task performance may influence the cardiovascular responses elicited and may vary by educational level. Other task characteristics, such as level of difficulty or salience to the participant, also may influence responses, although their relation to SES is unknown. Surprisingly few studies to date have directly examined the relation between cardiovascular reactivity and SES, and thus additional research is needed before firm conclusions can be made.

In the present study SBP reactivity in anticipation of exercise was related to greater stroke risk, whereas DBP reactivity was not. It is known that the sympathetic activation that occurs in the anticipatory phase before exercise is characterized by increased cardiac output without a compensatory decrease in vascular resistance. Moreover, SBP reactivity represents an acute increase in cardiac force during systole, whereas DBP reactivity reflects increases in resistance during diastole. Presumably, the pressor response patterns seen here in anticipation of exercise are representative of the sympathetic arousal experienced by these men to other emotionally stressful stimuli. Therefore, with repeated or prolonged exposure to stress, it may be that SBP reactivity and its accompanying increase in the rate and force with which blood is pumped into the vasculature exacerbates stroke risk by increasing the probability of an embolism.

Alternatively, the exaggerated SBP reactivity observed in this study may elevate the risk of stroke through general atherogenic mechanisms. For example, sympathetic arousal contributes to injury and dysfunction of the arterial endothelium, which may lead to formation of atherosclerotic plaques. In addition, neuroendocrine correlates of sympathetic nervous system activation, including increases in norepinephrine, epinephrine, and cortisol, can promote lipid mobilization and platelet activation, contributing to aggregation of platelets and formation of thrombi. Both of these processes also may exacerbate vascular injury and atherosclerotic plaque formation and progression. As noted previously, a well-recognized clinical complication of atherosclerosis is stroke.

We previously reported that the measure of stress-induced reactivity reported here is associated prospectively with increased risk of hypertension and progression of IMT in our population of middle-aged men from Finland. These certainly are plausible mechanisms by which reactivity increases risk of stroke. However, the design of our study does not make it possible to reliably test these hypotheses at this
time. The earlier reports were based on the subset of participants who completed the baseline and 4-year follow-up examinations of the KIHD Study. Of the 2303 participants included in the present analyses, <38% completed the 4-year follow-up, and among these respondents, there have been too few incident strokes since the follow-up examination to adequately examine the importance of these stroke risk factors. Continued follow-up will enable us to better model causal pathways between stress-induced reactivity, changes in risk factors over time, and incident stroke.

A few limitations of our study need to be noted. First, the demographic makeup of the sample precludes widespread generalization of the findings. Our study sample consisted only of middle-aged white men. Research is needed in female, minority, and nonwhite populations to determine whether similar relationships exist between stress-induced reactivity and excess risk of stroke. Prior research suggests that there may be important differences in cardiovascular responses to stress according to sex and race or ethnicity. It is critical to determine whether these different patterns of response are differentially related to cardiovascular disease risk. Moreover, stroke morbidity and mortality are greater in minorities than in whites, emphasizing the need for research on risk factors for stroke in nonwhite populations.

A second limitation is that we did not gather data on the acute versus chronic experience of stress among our participants. Such information would be valuable given that prolonged exposure to stress, resulting in frequent and intense stress responses, is thought to be importantly related to the development and progression of disease.

Our study also is limited by its inability to address the relation between stress-related reactivity and hemorrhagic stroke. A larger number of hemorrhagic strokes than occurred in our study population would be required to adequately assess the association between stress-induced cardiovascular reactivity and hemorrhagic strokes.

In summary, this study provides new epidemiological evidence of a link between stress-induced BP reactivity and an important clinical cerebrovascular end point in a population sample of middle-aged men. Additional research is needed to corroborate these findings in other populations, particularly in women and minorities. This is an important area of research to pursue, given the increasing prevalence of stroke in our aging population.

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References


vascular responses to stress on the progression of carotid atherosclerosis.


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Editorial Comment

Something Old and Something New

When considered separately from other cardiovascular diseases, stroke ranks as the third leading cause of death. It is a leading cause of serious, long-term disability in the United States. Identification of new risk factors holds promise for prevention of stroke’s substantial public health burden.

A longstanding hypothesis, called the cardiovascular reactivity hypothesis, is that individuals who show frequent, large blood pressure and heart rate responses to psychological stress experience recurrent sympathetic activation, which is unknown how the SBP rise in anticipation of exercise relates to accompanying hemodynamic and neuroendocrine changes, to the blood pressure response during exercise, and to total blood pressure burden via ambulatory blood pressure measurement. In this way, a more precise and generalizable interpretation of the present results can be made, results from ongoing epidemiological studies can be compared, and the best indicators of cardiovascular reactivity can be used as a diagnostic tool for stroke risk. It may be that a simple measure of SBP rise before exercise stress testing will be the most useful clinically, but we do not know yet.

Low socioeconomic status (SES) is a well-established predictor of cardiovascular diseases, including stroke, but the reason for this is not completely understood. Possible SES links involving cardiovascular reactivity to stress are that individuals from lower SES are more likely to respond to the same psychological stressors with larger cardiovascular responses than are higher SES individuals; low SES individuals and would show large SBP rises in a variety of other stressful circumstances. The next step in this research would be to confirm that assumption. Highly standardized and reliable measures of cardiovascular changes in response to diverse mental and physical challenges, eg, serial subtraction and cold pressor, are available to test the reactivity hypothesis. It is unknown how the SBP rise in anticipation of exercise tolerance testing relates to more conventional measures of reactivity and how reproducible it is. Blood pressure changes during exercise predict hypertension, and blood pressure rises before exercise stress testing predict hypertension in KIHD. It is important to evaluate how the anticipatory SBP exercise response relates to accompanying hemodynamic and neuroendocrine changes, to the blood pressure response during exercise, and to total blood pressure burden via ambulatory blood pressure measurement. In this way, a more precise and generalizable interpretation of the present results can be made, results from ongoing epidemiological studies can be compared, and the best indicators of cardiovascular reactivity can be used as a diagnostic tool for stroke risk. It may be that a simple measure of SBP rise before exercise stress testing will be the most useful clinically, but we do not know yet.

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are exposed to more frequent and severe psychological stressors, such that with other things being equal, they experience more frequent sympathetic nervous system activation; or that they experience more stressors and are more likely to be reactive to those stressors. The present study tested the first pathway and found that less-educated men showed greater rises in SBP before exercise. However, assuming that SES is in part a proxy for stress exposure, analyses testing the last pathway (whether less-educated men who were reactive to stress were at a particular disadvantage for stroke) did not reveal an interactive effect. Everson and her colleagues report the familiar and independent effect of education: men who were less educated had twice the risk of stroke relative to better-educated men. Educational attainment may not confer substantial advantage through any single risk factor, including cardiovascular reactivity. Rather, the health benefits of education may rest on the accumulation of lifelong exposures to multiple risk factors as well as on the resources for adapting to later life’s inevitable challenges.

So we have something old and something new in this article. Yet again, education remains a powerful predictor of stroke incidence, and we don’t know entirely why. Strong evidence is marshaled for a new risk factor for stroke: cardiovascular reactivity to psychological stress. This article encourages further testing of cardiovascular reactivity to mental stress in populations most vulnerable to stroke in the United States: elderly women, African Americans, and American Indians/Alaska natives.

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References
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