

Psychosocial Distress and Stroke Risk in Older Adults

Kimberly M. Henderson, BA; Cari J. Clark, ScD, MPH; Tené T. Lewis, PhD; Neelum T. Aggarwal, MD; Todd Beck, MS; Hongfei Guo, PhD; Scott Lunos, MS; Ann Brearley, PhD; Carlos F. Mendes de Leon, PhD; Denis A. Evans, MD; Susan A. Everson-Rose, PhD, MPH

Background and Purpose—To investigate the association of psychosocial distress with risk of stroke mortality and incident stroke in older adults.

Methods—Data were from the Chicago Health and Aging Project, a longitudinal population-based study conducted in 3 contiguous neighborhoods on the south side of Chicago, IL. Participants were community-dwelling black and non-Hispanic white adults, aged 65 years and older (n=4120 for stroke mortality; n=2649 for incident stroke). Psychosocial distress was an analytically derived composite measure of depressive symptoms, perceived stress, neuroticism, and life dissatisfaction. Cox proportional hazards models examined the association of distress with stroke mortality and incident stroke over 6 years of follow-up.

Results—Stroke deaths (151) and 452 incident strokes were identified. Adjusting for age, race, and sex, the hazard ratio (HR) for each 1-SD increase in distress was 1.47 (95% confidence interval [CI]=1.28–1.70) for stroke mortality and 1.18 (95% CI=1.07–1.30) for incident stroke. Associations were reduced after adjustment for stroke risk factors and remained significant for stroke mortality (HR=1.29; 95% CI=1.10–1.52) but not for incident stroke (HR=1.09; 95% CI=0.98–1.21). Secondary analyses of stroke subtypes showed that distress was strongly related to incident hemorrhagic strokes (HR=1.70; 95% CI=1.28–2.25) but not ischemic strokes (HR=1.02; 95% CI=0.91–1.15) in fully adjusted models.

Conclusions—Increasing levels of psychosocial distress are related to excess risk of both fatal and nonfatal stroke in older black and white adults. Additional research is needed to examine pathways linking psychosocial distress to cerebrovascular disease risk. (*Stroke*. 2013;44:000-000.)

Key Words: epidemiology ■ psychosocial stress ■ risk factors ■ women and minorities

Stroke is a leading cause of death and disability in the United States.¹ Diabetes mellitus, obesity, high blood pressure, cigarette smoking, and physical inactivity are widely recognized risk factors for stroke but they cannot account fully for the excess stroke risk observed in the population. Thus, research is needed to identify additional modifiable risk factors that may contribute to stroke risk. The literature on cardiovascular disease has clearly documented important associations between depression and cardiovascular outcomes, including stroke. Two recent meta-analyses concluded that depressive symptoms significantly increased stroke risk, particularly in women, but with most evidence from studies limited to whites.^{2,3} Recent research suggests, however, that cardiovascular risk may not be limited to specific negative mood states such as depression, but extends to psychosocial distress, a broader concept defined as the tendency to experience stress, negative events, and more generally a negative outlook on life.⁴⁻⁶ Less is known about the effect of psychosocial

distress on risk for stroke morbidity and mortality, although available evidence is suggestive. Recent findings from the INTERSTROKE study, an international multicenter case-control study in 22 countries, indicate that both depression and psychosocial stress, defined in that study as experiencing at least several periods of general stress at work or home in the past year, may be significant risk factors for stroke.⁷ Little information was provided on the measure of psychosocial stress in INTERSTROKE and a single item was used to assess depression. These 2 measures may be tapping into the same larger construct of distress and their relationship to stroke risk may be better assessed as such. Given that psychosocial distress may be modifiable, more research is needed to understand how it contributes to stroke risk.

This study uses data from the Chicago Health and Aging Project (CHAP) to investigate the risk of stroke mortality and incident stroke in relation to psychosocial distress in a population-based cohort of older black and white adults.

Received October 3, 2012; final revision received October 3, 2012; Accepted October 17, 2012.

From the Department of Medicine (K.M.H., C.J.C., S.A.E.-R.), Division of Biostatistics (H.G., A.B.), Biostatistical Design and Analysis Center, Clinical and Translational Science Institute (H.G., S.L., A.B.), University of Minnesota, Minneapolis, MN; Department of Epidemiology, Emory University, Atlanta, GA (T.T.L.); Department of Neurological Sciences and Rush Alzheimers Disease Center (N.T.A.), Rush Institute for Healthy Aging (N.T.A., T.B.), Department of Internal Medicine (D.A.E.), Rush University Medical Center, Chicago, IL; Department of Epidemiology, University of Michigan, Ann Arbor, MI (C.F.M.d.L.).

Correspondence to Susan Everson-Rose, PhD, MPH, University of Minnesota, 717 Delaware St SE, Suite 166, Minneapolis, MN 55414. E-mail saer@umn.edu

© 2012 American Heart Association, Inc.

Stroke is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.112.679159

We hypothesized that the effects of distress on stroke risk would be independent of demographic characteristics, stroke risk factors, and chronic conditions. Because stroke risk is known to vary by race, sex, and age, we further examined whether the relation of distress to stroke risk varied by these demographic characteristics.

Methods

Study Design and Population

CHAP is an ongoing, longitudinal study investigating Alzheimer disease and other chronic illnesses of the elderly. Sampling for CHAP took place in 3 adjacent neighborhoods within the south side of Chicago, IL, whose residents are predominantly black and non-Hispanic white adults from a broad range of socioeconomic backgrounds.⁸ Eligibility for participation in CHAP was based solely on age. All residents of the 3 targeted neighborhoods aged 65 years or older were invited to participate; 6158 participants (78.7% of eligible) completed baseline interviews between 1993 and 1996.

Baseline interviews were conducted in participants' homes and included questions on medical history, cognitive health, socioeconomic status, behavioral patterns, and psychosocial characteristics. Successive interviews were repeated in 3-year cycles after the baseline interview. The 2nd cycle (1997–1999) of interviews assessed the broadest range of psychosocial characteristics, and serves as the baseline for this analysis. A total of 4319 participants (87% of surviving cohort) completed cycle 2; of these, 4120 had nonmissing data on the psychosocial factors, demographic characteristics, and known vital status and thus were eligible for the current analyses. The Institutional Review Boards of Rush University Medical School and the University of Minnesota approved the study. All participants provided written informed consent.

Outcome Measures

Stroke Mortality

Information on vital status was obtained at each follow-up interview; reported deaths through 12/31/2007 were verified by linkages with the National Death Index. Primary, known causes of death were available for all National Death Index-verified deaths. Stroke deaths were defined by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) codes 430 to 438 for deaths before 1999, and Tenth Revision (ICD-10) codes I60–I69 beyond 1999. Stroke accounted for $\approx 9\%$ of deaths with known causes; 151 stroke deaths were identified over 6.7 (SD=3.5) years of follow-up.

Incident Stroke

Information on stroke hospitalizations within the CHAP cohort was ascertained via linkages with Medicare claims data from the Center for Medicare and Medicaid Services. Center for Medicare and Medicaid Services claims data were available through 12/31/2007; 88.2% of the CHAP cohort had matching claims data. Analyses of incident stroke excluded those who self-reported a history of stroke any time before the 2nd cycle of CHAP data collection (ie, baseline for the analyses). Participants also were excluded from analysis for incident stroke any time during follow-up when they were actively involved in a health maintenance organization because they would not simultaneously be enrolled in Medicare during those periods. Thus, for these analyses, the sample was reduced to 2649 participants. For the participants with claims data, strokes were defined by ICD-9 codes 430 to 438 because the Center for Medicare and Medicaid Services continues to use ICD-9 coding. Ischemic strokes were identified by ICD-9 codes 433.01, 433.1, 433.2, 433.21, 433.3, 433.31, 433.81, 434.01, 434.1, 434.11, 434.91, 435.2, 435.3, 435.8, 435.9, 436.0, 437.1, 437.7, 437.9, and 438.0. Hemorrhagic strokes were identified by ICD-9 codes 430, 431, 432.1, and 432.9. A total of 452 persons had at least 1 hospitalization for an incident stroke event (408 ischemic and 44 hemorrhagic) during follow-up; average follow-up time in these analyses was 6.0 (SD=3.4) years.

Measurement of Psychosocial Distress

Distress was measured by 4 psychosocial indicators at the 2nd cycle of CHAP data collection: depressive symptoms, perceived stress, neuroticism, and life satisfaction (reverse-coded). Previous analyses in CHAP showed that these 4 indicators loaded together on a single factor as a latent psychosocial construct that was theoretically and empirically justified and reliable across race and sex groups.⁹ Depressive symptoms were measured by the 10-item Center of Epidemiologic Studies-Depression scale, specifically developed for older populations;¹⁰ higher scores (range, 0–10) indicate more depressive symptoms (Cronbach alpha=0.76). Perceived stress was assessed by an abbreviated 6-item Perceived Stress Scale;^{11,12} higher scores indicate a higher level of perceived stress (Cronbach alpha=0.82). Life satisfaction was measured by the 5-item Life Satisfaction Scale,¹³ reverse-coded such that higher scores (range, 0–15) reflected life dissatisfaction (Cronbach alpha=0.73). Neuroticism, a broad personality domain characterized by anxious, angry, and vulnerable traits, was measured by 4 items from the NEO Five-Factor Inventory.¹⁴ Consistent with previous work,¹⁵ the scale score was multiplied by 3 to achieve consistency with the full, 12-item neuroticism scale (range, 0–45); higher scores reflect greater neuroticism. Shortening the scale resulted in a loss of internal consistency (Cronbach alpha=0.54); however, previous work shows that the abbreviated 4-item scale is significantly correlated with the full scale and equally predicts poor health outcomes.^{15,16}

A distress factor score was created by averaging the standardized values of the 4 psychosocial measures and dividing by its SD. A higher factor score was indicative of higher levels of distress.

Assessment of Covariates

Demographic characteristics obtained at the initial CHAP interview included self-reported age, race (non-Hispanic black or white), sex, and education (years of completed schooling). Stroke risk factors included as covariates were measured at the 2nd cycle of data collection. Body mass index was calculated as weight (kilograms) divided by height (meters) squared and modeled categorically based on clinically established body mass index categories.¹⁷ Systolic blood pressure (mm Hg) was measured as the average of 2 consecutive mercury sphygmomanometer readings, taken in the seated position.¹⁸ Self-reported cigarette smoking was reported as never, former (ever), and current. Physical activity was measured by the sum of 9 dichotomous response items inquiring about activities (eg, walking, gardening, dancing) over the last 2 weeks.¹⁹ History of chronic health conditions was based on affirmative responses to inquiries about 4 physician-diagnosed conditions: cardiovascular diseases, hip fracture, diabetes mellitus, and cancer;²⁰ each chronic condition was modeled separately as a dichotomous variable. History of stroke was indicated separately as a dichotomous variable based on self-reported, physician-diagnosed stroke. Chronic conditions and history of stroke took into account participants' reports from both the first and second cycles of data collection in CHAP. Self-reported current usage of antihypertensives, lipid-lowering medications, and antidepressants, confirmed by medication review, were modeled as 3 separate dichotomous variables.

Statistical Analysis

Descriptive statistics were calculated for baseline sociodemographic characteristics, distress, and health-related variables for all participants and by categorical distress scores. Cox proportional hazard models examined the association between distress at baseline and subsequent stroke mortality and incident stroke. Subsequent analyses examined incident ischemic and incident hemorrhagic strokes separately. The unit of time in all Cox models was 1 year; proportional hazards assumptions were checked analytically and graphically and all assumptions were met. Analyses for all outcomes were conducted in a similar manner, as follows. The initial model included adjustments for age, race, and sex. We also tested for age by distress, race by distress, and sex by distress interactions in a minimally adjusted model. The second model added covariates adjusting for education, body mass index, systolic blood pressure, smoking status, physical

activity, chronic conditions, and medication usage. Adjusted analyses for stroke mortality also included history of stroke. Because of missing data on some covariates, sample sizes for risk factor-adjusted models were 3916 for stroke mortality (142 events) and 2539 for incident stroke (426 events). Distress was modeled continuously and categorically (based on quartiles) in separate analyses. SAS software version 9.2 was used for all analyses.

Results

Population Characteristics

Baseline characteristics are shown in Table for all participants and by distress quartiles. The 4120 eligible participants were predominantly black and female, average age was 77 years old, most had a high school education, and an average of 1 chronic condition; 13.1% reported a history of stroke. Nearly all characteristics varied by distress level; those in the most distressed group (Q4) were older, more likely to be female and black, less educated, less physically active, and reported a higher prevalence of most chronic health conditions and use of antidepressants.

Distress and Stroke Mortality

Adjusting for age, race, and sex, each 1-SD higher distress score was significantly related to a 47% greater risk of dying

from stroke (hazard ratio [HR]=1.47; 95% CI=1.28–1.70; $P<0.0001$). Further adjustments for education, stroke risk factors, chronic conditions, medication usage, and history of stroke reduced the HR but the association remained significant (HR=1.29; 95% CI=1.10–1.52; $P=0.0018$). There were no age, race, or sex interactions with distress (all $P>0.20$; results not shown).

With distress modeled categorically and adjusting for age, race, and sex, participants in the highest quartile had nearly 3 times (HR=2.97; 95% CI=1.81–4.88; $P<0.0001$) and those in the third quartile had nearly 2 times (HR=1.98; 95% CI=1.19–3.30; $P=0.0091$) greater risk of dying from stroke relative to those with the lowest distress scores. The second quartile was not at increased risk (HR=1.24; 95% CI=0.71–2.15). Results from the risk factor-adjusted model are shown in Figure. The dose–response pattern of stroke mortality risk by level of distress is clearly evident; associations remained significant for the top 2 quartiles of distress.

Distress and Incident Stroke

Each 1-SD higher distress score predicted 18% greater risk of incident stroke during follow-up, adjusting for age, race, and sex (HR=1.18; 95% CI=1.07–1.30; $P=0.001$). Further

Table. Participant Characteristics at Baseline, 1997 to 1999

	All Participants (n=4120)	Quartiles of Distress				P Value
		Q1 (n=1032)	Q2 (n=1028)	Q3 (n=1031)	Q4 (n=1029)	
Age, mean (SD), y	77.1 (6.3)	75.7 (5.5)	76.7 (6.1)	77.5 (6.4)	78.5 (6.9)	<0.0001
Women, n (%)	2545 (61.8)	573 (55.5)	614 (59.7)	648 (62.9)	710 (69.0)	<0.0001
Black, n (%)	2531 (61.4)	587 (56.9)	566 (55.1)	642 (62.3)	736 (71.5)	<0.0001
Education, mean (SD), y	12.0 (3.7)	13.0 (3.6)	12.6 (3.5)	11.7 (3.6)	10.9 (3.6)	<0.0001
Systolic blood pressure, mm Hg, mean (SD)	135.0 (18.8)	136.3 (17.8)	135.0 (18.1)	134.9 (19.5)	133.6 (19.6)	0.019
BMI, kg/m ² , mean (SD)	26.7 (5.7)	27.1 (5.0)	26.9 (5.5)	26.7 (6.1)	26.3 (6.2)	<0.0001
BMI<18.5, n (%)	179 (4.4)	24 (2.4)	33 (3.2)	53 (5.2)	69 (7.0)	<0.0001
18.5≤BMI<25	1518 (37.5)	339 (33.0)	378 (37.1)	402 (39.5)	399 (40.3)	
25≤BMI<30	1381 (34.1)	421 (41.2)	362 (35.6)	318 (31.2)	280 (28.3)	
BMI≥30	971 (24.0)	239 (23.4)	245 (24.1)	245 (24.1)	242 (24.4)	
Smoking status, n (%)						0.043
Never smoker	1902 (46.2)	502 (48.7)	475 (46.2)	445 (43.2)	480 (46.7)	
Ever smoker	1719 (41.8)	420 (40.7)	439 (42.7)	433 (42.0)	427 (41.6)	
Current smoker	495 (12.0)	109 (10.6)	114 (11.1)	152 (14.8)	120 (11.7)	
Physical activity sum, mean (SD)	2.9 (4.8)	4.1 (5.4)	3.4 (5.3)	2.5 (4.6)	1.4 (1.1)	<0.0001
Use of antihypertensives, n (%)	2564 (62.2)	587 (56.9)	636 (61.9)	678 (65.8)	663 (64.4)	0.0002
Use of lipid-lowering medication, n (%)	443 (10.8)	134 (13.0)	122 (11.9)	104 (10.1)	83 (8.1)	0.002
Use of antidepressants, n (%)	152 (3.7)	12 (1.2)	31 (3.0)	38 (3.7)	71 (6.9)	<0.0001
Chronic health conditions, mean (SD)	1.2 (0.98)	0.97 (0.86)	1.2 (0.93)	1.3 (0.98)	1.4 (1.08)	<0.0001
History of CVD, n (%)	675 (16.4)	122 (11.8)	143 (13.9)	184 (17.9)	226 (22.0)	<0.0001
History of diabetes mellitus, n (%)	367 (8.9)	60 (5.8)	84 (8.2)	100 (9.7)	123 (11.9)	<0.0001
History of cancer, n (%)	941 (22.8)	204 (19.8)	252 (24.5)	241 (23.4)	244 (23.7)	0.051
History of hip fracture, n (%)	178 (4.3)	24 (2.3)	44 (4.3)	43 (4.2)	67 (6.5)	<0.0001
History of stroke, n (%)	538 (13.1)	83 (8.0)	117 (11.4)	128 (12.4)	210 (20.4)	<0.0001

BMI indicates body mass index. The study sample size was 4120, but because of missing data, the n for covariates ranged from 3988 to 4120. Q1 to Q4 indicate quartiles of the distress measure based on 4 approximate divisions of the overall distress factor score. Number of chronic health conditions is the count of a participant's history of cardiovascular diseases, hip fracture, diabetes mellitus, and cancer. Demographic statistics were similar for the sample populations included in the stroke mortality (n=4120) and incident stroke (n=2649) analyses. P values are from χ^2 tests or analysis of variance, as appropriate.

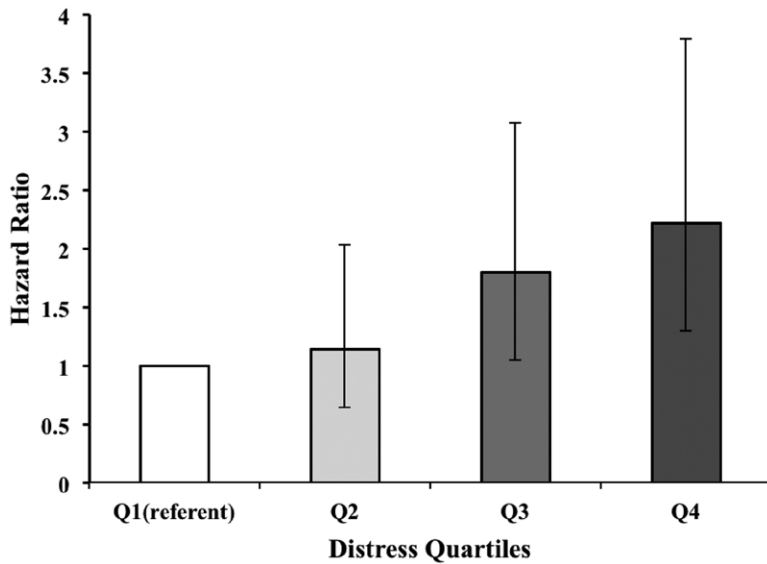


Figure. Hazard ratios and 95% confidence intervals (CIs) for stroke mortality by categories of distress. Q1 to Q4 indicate quartiles of the distress measure from low to high based on 4 approximate divisions of the overall distress factor score ($n=3916$, with 142 stroke deaths). **Error bars** indicate 95% CIs. The data in the graph are based on the risk factor-adjusted model, controlling for age, race, sex, education, systolic blood pressure, body mass index, physical activities, smoking status, chronic health conditions, medication usage, and history of stroke.

adjustment for education, stroke risk factors, chronic conditions, and medication usage attenuated these results (HR=1.09; 95% CI=0.98–1.21; $P=0.109$). There were no interactions between distress and age, race, or sex (all $P>0.12$; data not shown).

With distress modeled categorically, a dose–response pattern of risk for incident stroke was observed. Relative to the least distressed quartile, the HRs for the second, third, and fourth quartiles were 1.27 (95% CI=0.98–1.65; $P=0.067$), 1.44 (95% CI=1.10–1.87; $P=0.0068$), and 1.54 (95% CI=1.16–2.04; $P=0.0025$), respectively, in a model adjusted for age, race, and sex. Associations were reduced after adding adjustments for stroke risk factors (Q2: HR=1.21; 95% CI=0.93–1.58; $P=0.165$; Q3: HR=1.22; 95% CI=0.92 to 1.61; $P=0.16$; Q4: HR=1.31; 95% CI=0.97 to 1.76; $P=0.08$).

We further evaluated type of stroke in relation to distress, categorizing strokes into ischemic and hemorrhagic strokes as described. Distress was related to incident ischemic stroke in the minimally adjusted model (HR=1.12; 95% CI=1.01–1.24; $P=0.031$) but this relation was attenuated in the risk factor-adjusted model (HR=1.02; 95% CI=0.91–1.15; $P=0.69$). In contrast, a robust association of distress with hemorrhagic stroke was observed; each 1-SD increase in distress was associated with a 72% (HR=1.72; 95% CI=1.32–2.24; $P<0.0001$) increased risk of hemorrhagic stroke adjusting for age, sex, and race, which was little changed after risk factor adjustment (HR=1.70; 95% CI=1.28–2.25; $P=0.0003$).

Individual Psychosocial Measures and Stroke Outcomes

Finally, we examined the 4 individual psychosocial measures used to create the distress factor score in relation to stroke mortality and incident stroke. Each measure was modeled as a z score in separate analyses and covariates were the same as in our main analyses. For stroke mortality, HR were 1.34, 1.29, 1.36, and 1.47 for each 1-SD increase in depressive symptoms, neuroticism, life satisfaction (reverse-coded), and perceived stress, respectively (all $P\leq 0.001$), adjusted for age, race, and sex; with risk factor adjustments, the HR ranged from 1.19 to

1.27 (all $P\leq 0.05$). For incident stroke, the HR ranged from 1.11 to 1.13 (all $P<0.04$) in the minimally adjusted models and 1.05 to 1.08 and nonsignificant with risk factor adjustment. For incident hemorrhagic stroke, however, the adjusted associations were robust; HR were 1.63 ($P=0.0003$), 1.30 ($P<0.10$), 1.52 ($P<0.01$), and 1.74 ($P<0.001$) for depressive symptoms, neuroticism, life satisfaction, and perceived stress, respectively.



Discussion

This study identified a robust relationship between psychosocial distress and increased risk of stroke mortality and incident stroke in over 6 years of follow-up in a population-based cohort of older black and white adults. Moreover, a clear dose–response pattern of associations was evident, with the most distressed participants (top quartile of the distribution) experiencing more than a 2-fold increased risk of stroke mortality and a 31% increased risk of incident stroke, compared with their least distressed peers, after adjusting for potential confounders and stroke risk factors. Analyses of stroke subtypes revealed that distress was significantly related to incident hemorrhagic strokes, but not to ischemic strokes after adjustment for covariates. Our findings clearly document important adverse effects of psychosocial distress on cerebrovascular disease risk in the elderly.

Results from the present study are largely consistent with 3 other studies of stroke outcomes that had included measures labeled as psychological distress although the measures used in those studies mostly captured depressive symptoms. One study reported that high scores (≥ 5) on the 30-item General Health Questionnaire were associated with fatal but not non-fatal ischemic stroke or transient ischemic attacks in middle-aged men in South Wales.²¹ The General Health Questionnaire was described as a measure of psychological distress and high scorers were considered to possibly have a minor psychiatric disorder though the General Health Questionnaire was discussed largely as a measure of depressive symptoms. A more recent study used a 12-item version of the General Health Questionnaire and reported that high scorers had elevated risk

of death from cerebrovascular disease and ischemic heart disease over 8 years of follow-up among more than 68 000 British adults; incident stroke was not reported.²² Another large prospective cohort study of initially stroke-free middle-aged and older adults examined whether the association of mood status with stroke risk was related to symptoms of depression, measured by the 5-item Mental Health Inventory and labeled as distress, or to major depressive disorder and showed that only the symptom measure predicted increased stroke risk.² Our study found that a composite measure of distress, assessed by 4 indicators of psychosocial functioning, contributes to excess stroke risk. Each of the individual psychosocial measures related to our outcomes as well, at approximately similar levels of risk. This study extends the previous work by including a racially diverse cohort of older men and women.

The pathways by which distress may increase stroke risk are not fully understood. Interestingly, our analyses of incident stroke events show that the critical biological pathways may not be ischemic in origin. Several plausible pathways were not considered because of lack of data in the present study, but could help explain our observations. For example, chronic stress and negative emotional states have known neuroendocrine and inflammatory effects that could affect stroke risk.⁴ An extensive literature documents stress-induced dysregulation in various physiological systems, variously termed allostatic load or cumulative biological risk that could contribute to accelerated aging.^{9,23,24} Recent literature suggests that hypothalamic-pituitary-adrenal dysregulation related to stress and depression may cause an increase in circulating catecholamines, endothelial dysfunction, and platelet activation, culminating in a hypercoagulable state and thereby increasing stroke risk.^{25,26} These pathways likely are more important for ischemic than hemorrhagic stroke, however, and we observed much stronger findings for hemorrhagic stroke, so additional pathways need to be considered. It is possible that the burden of biological risk that occurs with chronic exposure to stress and distress leads to alterations in physiological regulation across multiple systems, which together could lead to the accumulation or exacerbation of cerebrovascular pathology and excess stroke risk of any subtype. Although no studies to date have tested this hypothesis, future analyses evaluating the relationship between multiple clinical neuroimaging markers of cerebrovascular disease (eg, infarct size, number, and location) to distress and incident stroke would be useful.

Psychological and behavioral factors also may be important. Persons who experience a high level of distress may be less likely or less able to adhere to treatment recommendations, for example, compliance with medications or maintaining a healthy lifestyle. Our most distressed participants were less physically active, and had a higher prevalence of cardiovascular disease and diabetes mellitus, suggesting potentially greater disease burden in this group, which could make lifestyle management more challenging. Nonetheless, controlling for these factors had little effect on the relation between distress and either stroke mortality or hemorrhagic strokes.

The present study has notable strengths and weaknesses. We included a sizable population-based sample of

older blacks and non-Hispanic whites from a large, urban Midwestern city, making our findings generalizable to other similar populations. However, findings may not hold in other minority or age groups. Moreover, because of differences in health outcomes across regions within the United States, our findings may not equally translate to other geographic regions. In particular, differences may occur in high-risk regions such as the southeastern region often regarded as the Stroke Belt. CHAP includes extensive data on sociodemographic characteristics and stroke risk factors, enabling us to conduct analyses with important multivariable adjustments. Yet, we lacked data on important inflammatory and neuroendocrine biomarkers, therefore limiting our ability to test additional important pathways that may link psychosocial distress to stroke risk. CHAP does not have concurrent imaging data on participants, which could provide important information and clinical details about the types of strokes experienced and potentially further our understanding of the observed relationships. This study does not have clinically adjudicated outcome data, although such data are rare in most large-scale epidemiological studies such as CHAP. Utilizing the Center for Medicare and Medicaid Services Medicare Claims data to ascertain incident stroke events (hospitalizations) in a study of persons 65 years and older has a distinct advantage, however, because there is little to no bias in outcome data attributable to differential healthcare access, which can be a problem in younger populations. Finally, with psychosocial assessments at just one point in time, we are unable to determine whether changes in distress levels occurred or if such changes influence stroke risk.

In sum, this study provides important evidence linking psychosocial distress to risk of both fatal and nonfatal stroke outcomes in elderly blacks and whites. The biological mechanisms underlying these associations remain to be determined, although our data suggest that pathways related to nonischemic disease mechanisms may be critical. Better understanding of the psychosocial risk pathways for cerebrovascular disease may lead to future interventions that could reduce the risk of stroke in the elderly.

Acknowledgments

The authors thank all participants in the Chicago Health and Aging Project, as well as all administrative and field staff for community development, oversight of project coordination, study coordination, and data collection.

Sources of Funding

This work was supported by National Institutes of Health (NIH) grants, including grant HL084209 from the National Heart, Lung, and Blood Institute (NHLBI), grant AG11101 from the National Institutes on Aging (NIA), and grant ES10902 from the National Institute on Environmental Health Sciences (NIEHS), grant K01HL092591 (Dr Lewis) from NHLBI, grant 1KL2RR033182-01 (Dr Clark) from the National Center for Research Resources (NCRR), grant 8UL1TR000114-02 from the National Center for Advancing Translational Sciences (NCATS), and by grant UL1RR033183 from NCRR to the University of Minnesota Clinical and Translational Science Institute (CTSI). Dr Everson-Rose also supported in part by grant 1P60MD003422 from the National Institute on Minority Health and Health Disparities (NIMHD). Contents of this paper are solely the responsibility of the authors and do not necessarily represent the

official views of the NIH, NHLBI, NIA, NIEHS, NIMHD, NCATS, NCR, or CTSI. The University of Minnesota CTSI is part of a national Clinical and Translational Science Award consortium created to accelerate laboratory discoveries into treatments for patients. Additional support provided by the Program in Health Disparities Research and the Applied Clinical Research Program (Dr Clark; Dr Everson-Rose; K.M. Henderson) at the University of Minnesota.

Disclosures

None.

References

- Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2–e220.
- Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB. Depression and risk of stroke morbidity and mortality: a meta-analysis and systematic review. *JAMA*. 2011;306:1241–1249.
- Dong JY, Zhang YH, Tong J, Qin LQ. Depression and risk of stroke: a meta-analysis of prospective studies. *Stroke*. 2011;42:188–196.
- Everson-Rose SA, Lewis TT. Psychosocial factors and cardiovascular diseases. *Annu Rev Public Health*. 2005;26:469–500.
- Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress. *Lancet*. 2007;370:1089–1100.
- Hamer M, Molloy GJ, Stamatakis E. Psychological distress as a risk factor for cardiovascular events: pathophysiological and behavioral mechanisms. *J Am Coll Cardiol*. 2008;52:2156–2162.
- O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al; INTERSTROKE investigators. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet*. 2010;376:112–123.
- Bienias JL, Beckett LA, Bennett DA, Wilson RS, Evans DA. Design of the Chicago Health and Aging Project (CHAP). *J Alzheimers Dis*. 2003;5:349–355.
- Clark CJ, Henderson KM, de Leon CF, Guo H, Lunos S, Evans DA, et al. Latent constructs in psychosocial factors associated with cardiovascular disease: an examination by race and sex. *Front Psychiatry*. 2012;3:5.
- Kohout FJ, Berkman LF, Evans DA, Cornoni-Huntley J. Two shorter forms of the CES-D (Center for Epidemiological Studies Depression) depression symptoms index. *J Aging Health*. 1993;5:179–193.
- Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385–396.
- Cohen S, Williamson G. Perceived stress in a probability sample of the United States. *The Social Psychology of Health: Claremont Symposium on Applied Social Psychology*. Newbury Park, CA: Sage; 1988.
- Diener E, Emmons RA, Larsen RJ, Griffin S. The Satisfaction With Life Scale. *J Pers Assess*. 1985;49:71–75.
- Costa PT, McCrae, R.R. *Revised NEO Personality Inventory (NEO-PI-R) and NEO Five-Factor Inventory (NEO-FFI) Professional Manual*. Odessa, FL: Psychological Assessment Resources; 1992.
- Wilson RS, Krueger KR, Gu L, Bienias JL, Mendes de Leon CF, Evans DA. Neuroticism, extraversion, and mortality in a defined population of older persons. *Psychosom Med*. 2005;67:841–845.
- Wilson RS, Barnes LL, Bennett DA, Li Y, Bienias JL, Mendes de Leon CF, et al. Proneness to psychological distress and risk of Alzheimer disease in a biracial community. *Neurology*. 2005;64:380–382.
- National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. *Obes Res*. 1998;6 suppl 2:51S–209S.
- Hypertension Detection and Follow-up Program Cooperative Group. Variability of blood pressure and the results of screening in the hypertension detection and follow-up program. *J Chronic Dis*. 1978;31:651–667.
- McPhillips JB, Pellettera KM, Barrett-Connor E, Wingard DL, Criqui MH. Exercise patterns in a population of older adults. *Am J Prev Med*. 1989;5:65–72.
- Cornoni-Huntley J, Brock D, Ostfeld A, Taylor J, Wallace R. *Established Populations for Epidemiological Studies of the Elderly Resource Data Book*. Washington, DC: US Department of Health and Human Services; 1986.
- May M, McCarron P, Stansfeld S, Ben-Shlomo Y, Gallacher J, Yarnell J, et al. Does psychological distress predict the risk of ischemic stroke and transient ischemic attack? The Caerphilly Study. *Stroke*. 2002;33:7–12.
- Hamer M, Kivimaki M, Stamatakis E, Batty GD. Psychological distress as a risk factor for death from cerebrovascular disease. *CMAJ*. 2012;184:1461–1466.
- Juster RP, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev*. 2010;35:2–16.
- King KE, Morenoff JD, House JS. Neighborhood context and social disparities in cumulative biological risk factors. *Psychosom Med*. 2011;73:572–579.
- Emsley HC, Hopkins SJ. Acute ischaemic stroke and infection: recent and emerging concepts. *Lancet Neurol*. 2008;7:341–353.
- Elkind MS. Why now? Moving from stroke risk factors to stroke triggers. *Curr Opin Neurol*. 2007;20:51–57.

Psychosocial Distress and Stroke Risk in Older Adults

Kimberly M. Henderson, Cari J. Clark, Tené T. Lewis, Neelum T. Aggarwal, Todd Beck, Hongfei Guo, Scott Lunos, Ann Brearley, Carlos F. Mendes de Leon, Denis A. Evans and Susan A. Everson-Rose

Stroke. published online December 13, 2012;

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2012 American Heart Association, Inc. All rights reserved.

Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://stroke.ahajournals.org/content/early/2012/12/13/STROKEAHA.112.679159>

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

Reprints: Information about reprints can be found online at:
<http://www.lww.com/reprints>

Subscriptions: Information about subscribing to *Stroke* is online at:
<http://stroke.ahajournals.org/subscriptions/>