Editorial

Psychological Distress as a Risk Factor for Stroke-Related Mortality

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In this issue, May et al report that psychological distress is a predictor of fatal ischemic stroke. What is “psychological distress”? It is a nonspecific term that encompasses sadness, frustration, anxiety, and a number of other negative mood states. It includes both mild and severe forms of these mood states, as well as both transient and persistent ones. It also refers both to symptoms of psychiatric disorders and to normal emotional responses to adversity.

Although several varieties of psychological distress have been investigated as potential risk factors for cardiovascular or cerebrovascular disease in community cohorts, and as risk factors for cardiac events, stroke, and mortality in patients with established coronary or cerebrovascular disease, distress is the variety of psychological distress that has received the most attention in all of these lines of research. Psychological distress, particularly in the form of depression, has a number of adverse effects in stroke patients. It impairs social functioning and quality of life and interferes with the recovery of motor and language functions. It may also be a risk factor for stroke and stroke-related mortality.

In a 14-year follow-up of 2201 middle-aged male participants in the Caerphilly study, May et al report that psychological distress, as measured at baseline by the 30-item version of the General Health Questionnaire (GHQ-30), was an independent risk factor for fatal ischemic stroke, after adjusting for potential confounds. In contrast, the hazard ratios for nonfatal ischemic stroke and for transient ischemic attack (TIA) were not statistically significant, even in univariate analyses. Because this is the first study to conduct separate analyses of fatal and nonfatal stroke, the findings represent a unique contribution to this line of research.

The results raise a number of questions about the relationship between psychological distress and stroke. First, in the Caerphilly cohort, as in many prospective studies of psychological risk factors for adverse health outcomes, we know something about the psychological state of the subjects at the time of enrollment but nothing about the course of their psychological distress over the follow-up interval. In this study, cerebrovascular events were ascertained as long as 14 years after the subjects were classified as either currently distressed or not distressed. Presumably, the risk of fatal ischemic stroke is related either to the cumulative exposure to psychological distress during the follow-up interval or to the level of distress just prior to the fatal event, not simply to the presence of distress at an essentially arbitrary point in time years before the event.

Furthermore, all we know about the psychological state of the subjects is that they were distressed at enrollment. We do not know, for example, how many of them had psychiatric disorders such as major depression or generalized anxiety disorder. Additional studies are needed in which standardized psychiatric interviews, along with questionnaires that assess depression and anxiety with higher specificity than the GHQ-30, are administered repeatedly over time. Such studies will be more complex and more difficult to implement than the Caerphilly study, but they are essential if we are to gain a thorough understanding of the parameters of exposure to psychological distress and of how and why exposure increases the risk of fatal ischemic stroke.

Second, why does psychological distress predict fatal ischemic stroke but not nonfatal stroke or TIA? The authors raise 2 distinct possibilities: The distressed subjects might have had more severe strokes than their nondistressed counterparts, or they might have had equally severe strokes yet, for some reason, had a higher case fatality rate. These explanations, in turn, point to 2 distinct directions for mechanistic research: Whereas the former would foster research on mechanisms that could promote more severe strokes in distressed individuals, the latter would require studies of interactions between psychological distress and factors that differentiate between fatal and nonfatal strokes. Unfortunately, data on stroke severity are not included in the report, so it is difficult to discern the more promising direction for future mechanistic research.

Nevertheless, mechanistic studies remain a high priority in this line of research, just as they are in research on the relationship between depression and cardiovascular morbidity and mortality. We have previously noted that despite the well-documented relationship between depression and cardiac morbidity and mortality, depression may not contribute to the onset or progression of coronary artery disease. An equally plausible explanation is that atherosclerosis develops and progresses for reasons unrelated to depression, and that depression increases the risk of cardiac events only in the presence of coronary artery disease, or perhaps only when the disease becomes clinically significant. Similarly, psychological distress may not promote the development of cerebrovascular disease, but it may instead heighten the risk of fatal stroke in patients with existing cerebrovascular disease.

Another explanation for the relationship between depression and stroke is that both may be caused by cerebrovascular disease. There is considerable interest in a possible link between late-onset depression and cerebrovascular disease. The “vascular depression hypothesis” proposes that depression in older adults may be caused or exacerbated by cerebrovascular disease. Brain imaging studies have documented both structural and functional brain abnormalities in patients with late onset depression. The present study, like...
some of the earlier studies, followed a cohort with no clinically apparent cerebrovascular disease at enrollment. However, given the age of the subjects at enrollment in this study (between 45 and 59 years), it is likely that some of them had occult cerebrovascular disease at that time. Whether “vascular depression” accounts for the findings is unclear, but it would be premature to discount this possibility.

The Caerphilly study is an excellent beginning, but the relationships between psychological distress and cerebrovascular disease, stroke, and stroke mortality deserve further investigation. High priorities include studies designed to (1) more precisely define exposure to psychological distress and (2) identify stroke characteristics such as infarct size or location that may differ between distressed and nondistressed cohorts; and to test mechanistic hypotheses about the relationships between stroke and depression and other forms of psychological distress. Clarification of the nature of the underlying mechanisms that link depression to increased risk for stroke mortality may enable clinicians to identify the depressed patients who are at greatest risk, as well as to target the most harmful components or concomitants of depression. Should depression contribute to the development of vascular disease, studies directed toward early prevention of disease progression should also be undertaken.

Finally, whether treating depression can reduce the risk of stroke mortality is not yet known. Effective treatment of depression has been shown to enhance quality of life and to improve physical, emotional, and social functioning. Thus, we strongly recommend that clinicians screen for and treat clinically significant depression as a problem in its own right, even if there is uncertainty as to whether treating depression can reduce the risk of stroke mortality.

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References
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