Stroke and Cognitive Decline
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**Stroke and cognitive impairment** are common among older persons. It is estimated that the lifetime risk for stroke is approximately 1 in 5 for women and 1 in 6 for men, and almost one-third of persons with stroke, which typically may involve motor, sensory, or other deficits, may have a significant degree of cognitive impairment within several months of the event. Furthermore, silent strokes are more common than clinically manifest stroke events but pose significant danger because they are harbingers of both future stroke and cognitive dysfunction. It is estimated that as many as 1 in 10 adults experience a silent stroke by their early 60s. Stroke and loss of cognitive vitality remain a substantial challenge, as there is a need to better understand the cellular and molecular mechanisms underlying cognitive impairment, course, and phenotypic manifestations of cognitive decline as well as the means to prevent this potentially devastating complication.

In this issue of *JAMA*, Levine and colleagues track trajectory of cognitive decline before and after incident stroke. In their analysis of data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) prospective cohort study, the authors obtained longitudinal but limited telephone cognitive testing in more than 23,000 study participants 45 years or older without baseline cognitive impairment. The primary outcome was change in global cognition as measured by the Six-Item Screener (SIS), a 3-item recall and 3-item temporal orientation test (score range, 0-6). Secondary outcomes were change in new learning (Consortium to Establish a Registry for Alzheimer Disease Word List Learning [score range, 0-30]), verbal memory (Word List Delayed Recall [score range, 0-10]), and executive function (Animal Fluency Test [number of animals named in 1 minute]).

Incident strokes were adjudicated by a team of experts, and a complex statistical analysis was carried out and included but was not limited to linear mixed-effects models. Comparisons were made between those with and without incident stroke.

During a median follow-up of 6.1 years, there were 515 incident strokes, of which 91% were ischemic, including 2.1% (n = 206 events) in white participants and 2.3% (n = 209 events) in black participants. As might be expected, those who experienced stroke were older men with more vascular risk factors, lower socioeconomic indicators, worse health status, and lower prestroke SIS scores. The main findings were that stroke was associated with an acute decline in global cognition (0.10 points [95% CI, 0.04-0.17]), new learning (1.80 points [95% CI, 0.73-2.86]), and verbal memory (0.60 points [95% CI, 0.13-1.07]), whereas executive function was not consistently shown to decline acutely. In addition, participants with incident stroke had statistically significantly faster declines in global cognition (0.06 points per year faster) and executive function (0.63 points per year faster) but not in new learning and verbal memory when compared with prestroke slopes (ie, rates). The poststroke rate of incident cognitive impairment occurred significantly faster when compared with the prestroke rate. Thus, acute cognitive decline was associated with incident stroke and accelerated and persisted over the approximately 6-year follow-up period.

This study by Levine and colleagues demonstrates that incident stroke is associated with an acute decline in global cognitive function based on a screening test (SIS) as well as acute decline in new learning and memory. A novel feature of the study is that its prospective design allowed for prestroke cognition to be tracked and provides rates of cognitive change prior to incident stroke. The displays of the slopes of cognitive function (Figure 2 in the article) are a powerful tool to help understand the findings and explain what may happen to cognition before and after stroke. Such figures may have relevance as an educational tool for a lay audience.

Even though some of the results of the statistical analysis show only modest, average cognitive loss, these findings may be interpreted as clinically meaningful because few persons can afford to lose any cognitive capacity over time. As the authors suggest, a decline of at least 0.5 standard deviations from baseline has been defined as clinically meaningful. A goal of large observational epidemiologic studies is to serve as a catalyst for future targeted investigations. In this case, such a study could identify which stroke subgroups show the most extensive cognitive decline.

However, the report by Levine et al does not provide information about the mechanism whereby stroke was associated with continued cognitive decline, the possible role of stroke and cardiovascular risk factors, possible interactions with neurodegenerative disease, and the means to prevent such decline. A prior longitudinal clinical-neuropsychological-neuroradiological correlative study of patients with stroke with and without cognitive impairment found little cognitive decline after the acute stroke period and up to 7 years among persons with stroke but without dementia at study entry. However, unlike the study by Levine and colleagues, the temporal point of comparison in the previous study was not prestroke cognition. Furthermore, in another study that featured magnetic resonance diffusion tensor imaging, there were dynamic changes of the white matter in either the affected or nonaffected brain hemisphere after stroke for up...
to several years. Others have also noted potential linkages between white matter integrity and vulnerability to cognitive decline and Alzheimer disease. These studies demonstrate the potential complexity of structural or anatomical changes that may underlie future cognitive change. It is likely that many different sources of prior damage to the brain (eg, stroke, trauma, hypertension, diabetes) increase vulnerability to subsequent brain disease, cognitive decline, and dementia.

Clinicians should remain alert for the presence of clinically manifest stroke or silent stroke identified incidentally on neuroimaging study, because these findings may be harbingers of future major complications such as recurrent stroke, cognitive impairment, and disability. Although there is no ideal office screening tool for detection of cognitive impairment after stroke, it may be reasonable to consider screening for cognitive impairment after stroke with the Montreal Cognitive Assessment. This instrument is valid, easy to administer, and highly sensitive. The routine cognitive screening of older community members has been criticized, but there is more support for screening persons at risk for cognitive decline. For example, the Canadian Best Practice Recommendations for Stroke Care support cognitive screening for persons with significant vascular risk factors for cognitive impairment. Information gained from cognitive screening can be used to plan for daily management of patient care based on cognitive performance and need for possible formal neuropsychological testing. In addition, intensification of vascular risk management may be indicated for patients at risk of cognitive impairment in an attempt to prevent subsequent stroke, myocardial infarction, loss of cognitive vitality, and overall disability.

ARTICLE INFORMATION
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REFERENCES