

Is sleep duration a risk factor for stroke?

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A total of 50 to 70 million Americans have a sleep or circadian disorder, with widespread consequences for health and safety.¹ Sleep health has become a national priority and a goal of the Healthy People 2020 program.² Observational and experimental studies demonstrate that poor sleep can lead to adverse health consequences.^{2,3} In particular, epidemiologic studies demonstrate associations between short sleep (≤ 5 –6 hours) and long sleep (≥ 8 –9 hours) durations with increased cardiovascular morbidity and mortality, compared to 7–8 hours of sleep.³

In this issue of *Neurology*®, Leng et al.⁴ report their findings from the European Prospective Investigation of Cancer (EPIC) study with 9,692 participants; their focus is the relationship between sleep duration and subsequent stroke over 9.5 years of follow-up. A unique aspect of the study is that in addition to sleep duration, they examined whether change in sleep duration up to 4 years after baseline was associated with stroke incidence. The investigators also conducted an updated systematic review and meta-analysis of longitudinal population studies that reported on the association between sleep duration and stroke, including results from the EPIC study. The results from the meta-analysis showed both short and long sleep durations to be associated with the incidence of stroke.

The association between short sleep duration and stroke is not surprising given that experimental sleep restriction compromises insulin sensitivity, raises blood pressure, and increases total and low-density lipoprotein cholesterol levels.^{5,6} Short sleep duration is also associated with obesity, diabetes, hypertension, hypercholesterolemia, and the metabolic syndrome,^{5,6} all potent risk factors for stroke. In their analysis of EPIC data, Leng et al. found no definitive relationship between short sleep and stroke incidence. These results are in agreement with previous findings of a much weaker link in elderly subjects between short sleep duration and cardiometabolic parameters such as obesity and hypertension.^{5,6}

The association between long sleep duration and stroke poses a conundrum given the lack of evidence that sleeping for longer than 8 hours has adverse health effects, with no published laboratory or epidemiologic studies demonstrating a possible mechanism identifying long sleep as a cause of morbidity.⁶ Long sleep duration could be an epiphenomenon of stroke as opposed to a cause. Long sleep duration is associated in cross-sectional studies with inflammation,⁷ carotid artery atherosclerosis,⁸ and left ventricular mass,⁹ all of which are strong risk factors for stroke and cardiovascular disease. It is plausible that the associations between long sleep duration and the incidence of stroke in epidemiologic studies have been confounded by risk factors (i.e., sleep apnea, inflammatory markers) that were not measured and controlled for in multivariable analyses. Future studies would ideally control for these factors, and determine if these explain or mediate the association between long sleep duration and stroke.

Intriguingly, in their EPIC analyses, Leng et al.⁴ found long sleep duration to be associated with stroke incidence only in subjects aged 63 years and older. Sleep durations measured before the occurrence of stroke may be influenced by medical conditions that had eventually predisposed the patients to increased stroke risk. This is particularly relevant in the elderly for whom sleep duration may be shortened or lengthened as the result of medical factors and may not represent sleep over the course of their lifetimes.^{5,6} The investigators also found that participants whose sleep durations were persistently long or changed from short to long were more than twice as likely to have a subsequent stroke compared to those with persistently average sleep durations. Long sleep duration could therefore be a harbinger of stroke through its associations with potent cardiovascular risk factors. Lengthening sleep duration could portend strokes and serve as an early warning sign, suggesting the need for further diagnostic testing or for taking precautionary measures.

See page 1072

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