Humans are social animals. The quality and quantity of our relationships with other humans (social network) underpin our happiness and success.¹ A social network structure also provides functional social support. It assists us emotionally and physically, informs and educates us, and improves our health-related choices and behaviors.² But does it protect us from stroke?

Several epidemiological studies have reported small social network and limited social support to be associated with an increased incidence of mortality, coronary heart disease, cancer, and mood disorders,³⁻¹³ but only 4 studies have examined the association with stroke and the results are conflicting.³⁻⁶,¹⁴,¹⁵

In the first study, of 2603 members of a US health maintenance organization, there was no difference in the 15-year incidence of stroke among those in the lowest versus highest tertile of social network indices.⁵

However, in the second study, of 32624 US male health professionals, socially isolated men had an increased risk of stroke (relative risk, 2.21; 95% confidence interval [CI], 1.12⁻⁴.35), which was dose-dependent (P for trend=0.008).⁶ A subsequent study of 629 women with suspected myocardial infarction also found a higher rate of stroke among those with more socially isolated women than those with more social relationships (adjusted hazards ratio [HR], 2.7; 95% CI, 1.1⁻⁶.7).¹⁴ Finally, among 44152 Japanese men and women, those lacking someone to share intimate personal feelings and secrets had a higher incidence of stroke (adjusted HR, 1.18; 95% CI, 1.01⁻¹.37).¹⁵

Having no friends (adjusted HR, 0.98; 95% CI, 0.80⁻¹.20) and no esteem support (adjusted HR, 1.16; 95% CI, 0.99⁻¹.37) were not associated with a higher incidence of stroke, however; nor was low social support (HR, 1.11; 95% CI, 0.89⁻¹.37).¹⁵

In this issue of Stroke, Nagayoshi et al¹⁶ report that a small social network was associated with a 44% increased risk of stroke (HR, 1.44; 95% CI, 1.02⁻².04) compared with a large social network in the Atherosclerosis Risk in Communities (ARIC) study. This result incorporates adjustment for the higher likelihood of being black, male, unmarried, unemployed, less educated, diabetic, a smoker, and scoring highly on the vital exhaustion measure among the 380 participants (2.8%) with a small social network compared with a large social network.¹⁶

The association appeared to be partly mediated by perceived social support and vital exhaustion (fatigue, irritability, and feelings of demoralization) but not inflammation (high-sensitivity C-reactive protein). There was no significant increase in the incidence of stroke among the few participants (0.5%) who perceived a lack of social support compared with those with high social support (HR, 1.59; 95% CI, 0.75⁻³.36).¹⁶

The internal validity of the ARIC study results is supported by the rigorous study methodology. A large cohort (n=13686) of community-dwelling, biracial, middle-aged, stroke-free men and women were recruited prospectively from sampling 4 US communities and underwent a standardized baseline assessment of candidate variables (social network by the 10-item Lubben Social Network Scale, and perceived social support by a 16-item Interpersonal Support Evaluation List-Short Form) and covariates.¹⁶ After a median of 18.6 years follow-up, a large number (n=905) of incident stroke outcomes were adjudicated according to a standardized definition of stroke. The limitations of the study include measurement of social network and support based on self-report and at one point in time only, probable incomplete ascertainment of stroke outcome events (hospitalized or fatal strokes reported by participants and proxys), and limited statistical power to evaluate the effect of a perceived lack of social support on stroke risk because of its low prevalence (0.5%) in the study population.

The external validity of the ARIC study results is supported by their consistency with other studies.⁶,¹⁴,¹⁵ The results of the first study of 2603 health maintenance organization members⁵ may also have been consistent if the authors of that study had not defined a small social network as a score in the lowest tertile, because this may have been too crude a subcategorization if the prevalence of a small social network was well below one third, as observed in the ARIC study.¹⁶

Overall, the totality of published evidence suggests that a small social network is a risk factor for incident stroke. The association is reasonably strong, consistent, specific, and plausible. The potential mechanisms by which social interaction and relationships may reduce stroke risk include behavioral, social, psychological, and physiological pathways. Individuals with a small social network and support are predisposed to adverse health behaviors (eg, cigarette smoking, alcohol and other drug abuse, poor diet, sedentary lifestyle) and suboptimal health service utilization and adherence to medical recommendations.² Small social network is also associated with psychological stress, activation of the neuroendocrine system,
upregulation of chronic inflammation, and endothelial and platelet dysfunction.\(^{17,18}\)

Nevertheless, it is not possible to prove a causal relationship between small social network and stroke from observational studies.\(^{19}\) The results above may reflect residual confounding by failure to accurately measure and adequately adjust for factors such as diet, mood, health service utilization, and other complex social and environmental exposures that may have differed between the comparison groups (small versus large social network) and the outcome (stroke). The results may also reflect bias, such as reverse causality bias whereby lifestyle choices and health-related behaviors may have determined social networks.

More robust techniques for assessing causal associations between social network and stroke are needed. Randomized controlled trials are problematic in this context.\(^{20}\) However, observational Mendelian randomization studies may be possible.\(^{21}\) Although the genetic and biological mechanisms underlying social networking are not well understood, the neuropeptides oxytocin and arginine vasopressin are brain signaling molecules that encode proteins that regulate a suite of social behaviors relevant to social bonding.\(^{22,23}\) Genetic polymorphisms in oxytocin pathway genes (eg, CD38 [rs12644506]) may influence social integration and other social behaviors.\(^{24}\)

To perform Mendelian randomization, such genetic variants require 3 key features: first, to be allocated to individuals randomly (ie, at conception); second, to be associated with the risk factor (social network); and third, to affect outcome (stroke) only via the risk factor and not other biological pathways.\(^{25}\)

While awaiting more definitive studies of a causal association between social network and stroke risk, it would be appropriate to encourage health professionals to consider social network size and quality as a possible causal and modifiable risk factor for stroke, to help individuals at risk of stroke to become more socially engaged and to advocate for more community resources to facilitate social networks.

Disclosures

None.

References

Social Network and Stroke Risk: Size Matters
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Stroke. 2014;45:2853-2854; originally published online August 19, 2014;
doi: 10.1161/STROKEAHA.114.006798
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 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/45/10/2853

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