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Featured Article

Associations between social relationship measures, serum brain-derived neurotrophic factor, and risk of stroke and dementia

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Abstract

Introduction: Mechanisms underlying social determinants of stroke and dementia are unclear and brain-derived neurotrophic factor (BDNF) may contribute as a molecular link.
Methods: Using the Framingham Study, we examined social relationship measures as predictors of higher serum BDNF level and cumulative incidence of stroke and dementia.
Results: Among 3294 participants, controlling for age and sex, isolation trended with lower BDNF (odds ratio = 0.69 [0.47–1.00]). Participants with more companionship had reduced risk for stroke (hazard ratio [HR] = 0.59 [0.41–0.83]) and dementia (HR = 0.67 [0.49–0.92]). Greater emotional support was associated with higher BDNF (odds ratio = 1.27 [1.04–1.54]), reduced dementia risk (HR = 0.69 [0.51–0.94], and among smokers, reduced stroke risk (HR = 0.23 [0.10–0.57]). Associations persisted after additional adjustments. BDNF partly mediated the total effect between emotional support and dementia risk.
Conclusions: Availability of social support appears to be associated with increased BDNF levels and, in certain subsets, reduce risk of subsequent dementia and stroke, thus warranting study of these pathways to understand their role in neuroprotection.

Keywords: Brain-derived neurotrophic factor; Social relationships; Social support; Social networks; Dementia; Stroke; Epidemiology; Cohort studies

1. Introduction

Social environments, particularly social relationships, are strongly linked with physical and mental health [1]. However, little is known about the neurobiological mechanisms underlying the association of social relationships and healthy cognitive aging [2,3]. Because lower circulating BDNF levels and small social networks have separately been associated with higher risk of incident stroke [3,4], cognitive dysfunction [2,5,6], and the accumulation of Alzheimer's disease pathology [7,8], we postulated that BDNF may be a biological link between social relationships and a reduced likelihood of developing stroke or dementia. Brain-derived neurotrophic factor (BDNF) may partly mediate observed associations

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given that it is a neuroprotective molecule critical for synaptic plasticity and neuronal repair [9], which is inducible by lifestyle factors [10,11] and, in animal models, social enrichment [12]. BDNF crosses the blood-brain barrier with high capacity and is highly stable over time, thus serum BDNF is reflective of central nervous system levels [5,13,14]. Our study is motivated by the overarching hypothesis that social relationships alter the biology of the brain and are crucial to reducing stroke and dementia risk through a pathway that involves BDNF, as suggested by the observed effect of social enrichment in animal models and BDNF's association with reduced risk of stroke and dementia-related neuropathology. To our knowledge, there has been no clinical study to date that has systematically examined the associations between social relationships and BDNF in humans as well as how these associations might influence the risk for stroke and dementia. We analyzed a sample from the Framingham Heart Study (FHS)—one of the longest running and most closely monitored community-based cohort studies in the United States—to investigate the association between social relationships, serum BDNF, and risk for stroke and dementia.

2. Methods

2.1. Standard protocol approvals, registrations, and patient consents

Written informed consent was obtained from all participants. The Institutional Review Board of Boston University Medical Center approved the consent form and original study design.

2.2. Participants

We used data from the community-based, prospective FHS Original (n = 5209, initiated 1948) and Offspring (n = 5124, initiated 1978) cohorts from the general community of Framingham, Massachusetts (Fig. 1). For additional details about the FHS, see previous publications [15]. The analytic group was derived from the 703 Original cohort participants who attended the 23rd biennial examination (1992–1996) and the 3432 who attended the seventh Offspring examination (1998–2001)—when serum samples were drawn for BDNF measurement—and were followed for a median 11 years (range up to 16 years) with minimal loss to follow-up. At examination, 3920 of 4135 (95%) had social relationships assessed and 3294 of 3920 (84%) also had serum drawn for BDNF measurement. For analysis of dementia, persons aged <60 years, those with prevalent dementia, or lack of follow-up for dementia were excluded. For analysis of stroke, those who were aged <45 years, had prevalent stroke, or did not have stroke follow-up were excluded. Thus, a total of 3294 participants were available for cross-sectional analysis of association between social relationships and BDNF, 1834 participants were available for retrospective analyses of association with dementia, and 3210 participants were available for retrospective analyses of association with stroke. On the basis of the effect sizes observed in a previous study that examined association between social relationships and biomarkers of inflammation

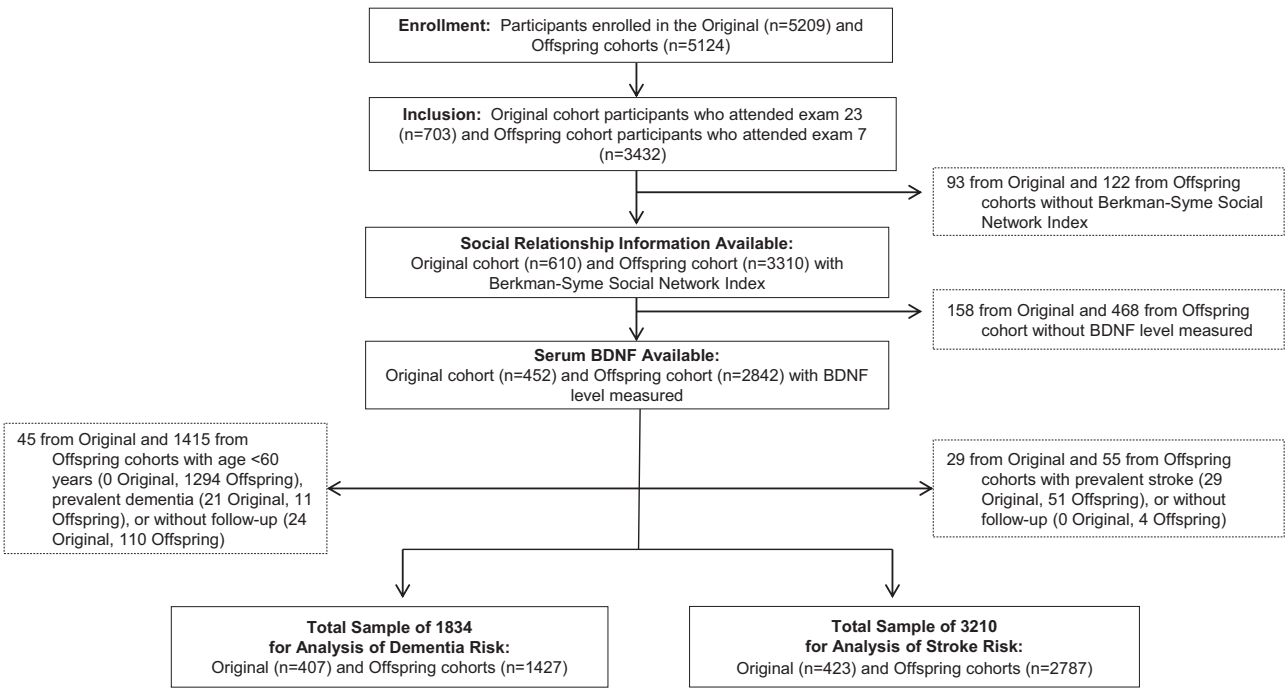

Fig. 1. Derivation of analytic sample used in each analysis. Abbreviation: BDNF, brain-derived neurotrophic factor.