Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.
Methods. MRI Quantification of Total Cerebral Volume

Acquisition Parameters
Imaging was performed with a Siemens Magnetom 1.0 Tesla field strength magnetic resonance machine using a double spin-echo coronal imaging sequence of 4 millimeter contiguous slices from nasion to occiput with repetition time of 2,420 msec, echo time (TE) of TE1 20/ TE2 90 msec; echo train length 8 msec; field of view 22 cm and a 182 × 256 acquisition matrix interpolated to a 256 × 256 with one excitation. Approximately 90% of scans were performed in Massachusetts; the remainder were performed out-of-state and used a 1.5T machine with identical scan protocol. Off-site scanners had test scans with verification that they were performed correctly according to the Framingham Study MRI scan protocol.

Image Analysis
MRI scan digital information was transferred after acquisition to the central laboratory directed by a co-author (CD) for processing and analysis. Analyses were all conducted blind to participant identifying information. Images were evaluated with semiautomatic segmentation analyses using operator-guided removal of non-brain elements by operator-guided tracing of the dura matter within the cranial vault. This included the middle cranial fossa and was above the posterior fossa and cerebellum. The cranial vault measure derived was defined as total cranial volume and was used as a head size estimate to correct for established sex differences in head size.

Total cerebral brain volume was quantified using a multi-step process starting with image segmentation to define brain matter from cerebral spinal fluid (CSF). Subtraction of the second echo image from the first echo image yielded a difference image. Following image segmentation into brain matter and CSF, the operator returned to the image to measure lobar brain volumes. To preserve measurement precision, segmented brain-CSF images were rotated separately from the original image.

The image was transformed into anatomic standard space; the operator then returned to the image and identified brain lobar and regional CSF measures. Volumes were all calculated as the sum of the pixels within the identified region of interest multiplied by the pixel volume in milliliters. Repeat analysis of intra- and inter-rater reliabilities were consistently above 0.90. The measured total cerebral volume was corrected for head size using the ratio of total cerebral volume over total cranial volume, multiplied by 100.
### eTable 1. Cognitive Tasks and Standardization Used to Create the Global Cognitive Score

| Cognitive Task                  | Natural Log-Transformations | Standardizing Formula<sup>b</sup> | Component Loading<sup>c</sup> |
|---------------------------------|----------------------------|----------------------------------|-----------------------------|
| Trails Making Test A            | -log(score)                | (score − 0.68) / 0.34            | 0.13                        |
| Trails Making Test B            | -log(score)                | (score + 0.22) / 0.45            | 0.18                        |
| Trails Making Test (B − A)      | -log(2 + score)            | (score + 1.03) / 0.22            | 0.16                        |
| Logical Memory – Immediate Recall |                             | (score − 11.55) / 3.4           | 0.14                        |
| Logical Memory – Delayed Recall  |                             | (score − 10.61) / 3.59          | 0.15                        |
| Visual Reproductions – Immediate Recall | | (score − 9.07) / 3.15 | 0.17                        |
| Visual Reproductions – Delayed Recall |             | (score − 8.2) / 3.36          | 0.18                        |
| Paired Associate Learning – Delayed Recall |           | (score − 8.3) / 1.46 | 0.13                        |
| Hooper Visual Organization Test | -log(31 − score)           | (score + 1.65) / 0.52            | 0.14                        |
| Similarities Test               |                             | (score − 16.77) / 3.55          | 0.14                        |

<sup>a</sup> Adapted from Pase et al. 2016.<sup>33</sup>

<sup>b</sup> Natural log transformed cognitive tasks were used to create the standardized variables where applicable.

<sup>c</sup> Global cognitive score calculated by summing the products of the standardizing formulas and the component loadings for each cognitive task.
**eTable 2. Sample Distribution of Five Social Support Domains, Stratified By Level**

| Social Support Domain* (n=2171) | No. of Participants (%) |
|----------------------------------|-------------------------|
| **Listener**                     |                         |
| None of the time                 | 10 (1%)                 |
| Little of the time               | 79 (4%)                 |
| Some of the time                 | 181 (8%)                |
| Most of the time                 | 748 (35%)               |
| All of the time                  | 1150 (53%)              |
| **Advice**                       |                         |
| None of the time                 | 26 (1%)                 |
| Little of the time               | 99 (5%)                 |
| Some of the time                 | 289 (13%)               |
| Most of the time                 | 850 (39%)               |
| All of the time                  | 901 (42%)               |
| **Love-Affection**               |                         |
| None of the time                 | 23 (1%)                 |
| Little of the time               | 98 (5%)                 |
| Some of the time                 | 146 (7%)                |
| Most of the time                 | 502 (23%)               |
| All of the time                  | 1394 (65%)              |
| **Emotional support**            |                         |
| None of the time                 | 20 (1%)                 |
| Little of the time               | 87 (4%)                 |
| Some of the time                 | 184 (9%)                |
| Most of the time                 | 700 (32%)               |
| All of the time                  | 1175 (54%)              |
| **Sufficient contact**           |                         |
| None of the time                 | 29 (1%)                 |
| Little of the time               | 112 (5%)                |
| Some of the time                 | 244 (11%)               |
| Most of the time                 | 725 (34%)               |
| All of the time                  | 1056 (49%)              |

*For each type of social support, participants responded to the following items on the Berkman-Syme Social Network Index: listening, “Can you count on anyone to listen to you when you need to talk?”; advice, “Is there someone available to give you good advice about a problem?”; love-affection, “Is there someone available to you who shows you love and affection?”; emotional support, “Can you count on anyone to provide you with emotional support?”; and, sufficient contact, “Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide?”.
### eTable 3. Total Cerebral Volume and Global Cognition Residuals as a Function of Five Social Support Domains*

| Models b | TCV-r | GCS-r |
|----------|-------|-------|
|          | Beta Estimate (SE) | P Value | Beta Estimate (SE) | P Value |
| Overall (n=2171) | | | | |
| Listener | 0.14 (0.03) | .03 | 0.16 (0.06) | .02 |
| Advice | 0.17 (0.05) | .002 | 0.05 (0.05) | .40 |
| Love-Affection | 0.09 (0.07) | .19 | 0.06 (0.07) | .37 |
| Emotional support | 0.11 (0.06) | .09 | 0.04 (0.06) | .56 |
| Sufficient contact | 0.11 (0.06) | .04 | 0.05 (0.06) | .35 |
| Age <65 (n=1273) | | | | |
| Listener | 0.14 (0.08) | .07 | 0.01 (0.08) | .91 |
| Advice | 0.11 (0.07) | .12 | -0.06 (0.06) | .35 |
| Love-Affection | 0.10 (0.08) | .19 | 0.09 (0.07) | .24 |
| Emotional support | 0.09 (0.08) | .28 | 0.01 (0.07) | .88 |
| Sufficient contact | 0.10 (0.07) | .15 | 0.03 (0.06) | .65 |
| Age ≥65 (n=898) | | | | |
| Listener | 0.14 (0.11) | .18 | 0.37 (0.12) | .001 |
| Advice | 0.25 (0.09) | .005 | 0.20 (0.10) | .04 |
| Love-Affection | 0.06 (0.12) | .60 | 0.01 (0.12) | .93 |
| Emotional support | 0.14 (0.10) | .19 | 0.07 (0.11) | .51 |
| Sufficient contact | 0.15 (0.10) | .13 | 0.10 (0.11) | .37 |

Abbreviations: TCV-r, total cerebral volume residual; GCS-r, global cognitive score residual.

* To account for covariates, all models use the residuals of total cerebral volume and global cognitive scores regressed onto the primary set of covariates: age, age^2, sex, education, and time interval from collection of social support measures to time of MRI and neuropsychological testing. Multivariable regressions separately modeled TCV-r and GCS-r as a function of five different domains of social support.

b Each type of social support domain was included as a predictor in separate models above and as a two-level variable, high versus low. A high level was defined as responding “most of the time or all of the time” versus “some, little, or none of the time” for the respective item:
- Listener, “Can you count on anyone to listen to you when you need to talk?”
- Advice, “Is there someone available to give you good advice about a problem?”
- Love-affection, “Is there someone available to you who shows you love and affection?”
- Emotional support, “Can you count on anyone to provide you with emotional support?”
- Sufficient contact, “Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide?”
**eTable 4. Multivariable Models of Global Cognition as a Function of Cerebral Volume and Five Listener Availability Levels**

| Level of Supportive Listener Availability<sup>b</sup> | No. of Participants (overall) | Level-Specific Beta Estimate (SE) | P Value |
|-----------------------------------------------------|-------------------------------|----------------------------------|---------|
| None of the time                                     | 10                            | -0.23 (0.30)                     | .48     |
| Little of the time                                   | 79                            | 0.20 (0.11)                      | .07     |
| Some of the time                                     | 181                           | 0.21 (0.08)                      | .006    |
| Most of the time                                     | 748                           | 0.09 (0.04)                      | .02     |
| All of the time                                      | 1150                          | 0.08 (0.03)                      | .006    |

<sup>a</sup> To account for covariates, all models use the residuals of total cerebral volume and global cognitive scores regressed onto the primary set of covariates: age, age², sex, education, and time interval from collection of social support measures to time of MRI and neuropsychological testing. Multivariable regressions modeled global cognitive score residuals as a function of total cerebral volume residuals. Data are presented as beta estimate in standard deviation units and standard error (SE).

<sup>b</sup> Response to the item, “Can you count on anyone to listen to you when you need to talk?”
eFigure 1. Predicted Association Between Cerebral Volume and Global Cognition By Availability of Supportive Listening: All Participants

To account for covariates, models are based on the residuals of total cerebral volume and global cognitive scores when regressed onto the primary set of covariates: age, age², sex, education, and time interval from social support assessment to visit when MRI and neuropsychological testing were obtained. Blue line=High listener availability (n=1898), Red line=Low listener availability (n=279). Bands indicate 95% confidence intervals.
To account for covariates, models are based on the residuals of total cerebral volume and global cognitive scores when regressed onto the primary set of covariates: age, age², sex, education, and time interval from social support assessment to visit when MRI and neuropsychological testing were obtained. Blue line=High listener availability (n=786). Red line=Low listener availability (n=110). Bands indicate 95% confidence intervals.
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