

Association between early adulthood/midlife stressors and later-life neuroimaging markers

Kaiser Permanente Research

Molly R. LaPoint¹, Sirena Gutierrez², Joseph N. Roscoe¹, Rachel A. Whitmer³, Lisa L. Barnes⁴, Eleanor Hayes-Larson⁵, Sarah Tomaszewski Farias³, Charles S. DeCarli³, Elizabeth Rose Mayeda⁶, M. Maria Glymour⁷, Maria M. Corrada⁸, Paola Gilsanz¹

(1) Kaiser Permanente Northern California Division of Research, Pleasanton, CA; (2) University of California, San Francisco, San Francisco, CA; (3) University of California, Davis, Davis, CA; (4) Rush Alzheimer’s Disease Center, Chicago, IL; (5) University of Southern California, Los Angeles, CA; (6) University of California, Los Angeles, Los Angeles, CA; (7) Boston University, Boston, MA; (8) University of California, Irvine, Irvine, CA

Background

Midlife stress increases dementia risk but its association with later-life markers of neurodegeneration and vascular injury remains unclear, particularly in diverse populations.

Objective

Investigate potential associations between early/midlife stressful life experiences and brain health at older ages.

Methods

- Participants came from 3 cohort studies in Northern California (KHANDLE, STAR, LA90).
- Early/midlife stressors (ages 25-58) were assessed using survey items on whether they were currently (at the time of the survey) experiencing “serious or disturbing problems” in 5 domains: marriage, family, drugs, job, and finances.
- Stressors were categorized into 3 binary measures:
 - Overall stressors (any domain)
 - Interpersonal stressors (marriage or family)
 - Resource stressors (job or finances)
- MRI outcomes (ages 60-103) included z-scored volumetric measures adjusted for intracranial volume and z-scored and log transformed white matter hyperintensities (WMH).
- Utilized linear models adjusting for age at imaging, years between MRI and midlife survey, demographics and cohort.
- Selection weights were estimated to account for differential participation in brain imaging, based on demographics and self-rated health (in KHANDLE and STAR).

Results

- 71 (24%) of participants experienced stressors. 33 (9%) experienced interpersonal stressors and 52 (14%) experienced resource stressors.
- In unweighted models, experiencing any stressors was associated with larger temporal lobe volume ($\beta=0.26$, 95% CI [0.03, 0.50]). This relationship was attenuated in weighted models ($\beta=0.18$, 95% CI [-0.06, 0.42]).

The forest plot displays point estimates (z-scored) for brain volume across eight regions: gray, hippocampal, frontal, occipital, parietal, temporal, ventricular, and log WMH. The y-axis represents the Point Estimate (z-scored) ranging from -0.3 to 0.3. The x-axis is labeled Brain Volume. The plot is organized into three rows: overall, interpersonal, and resource stressors. Each row has two columns: unweighted and weighted models. The overall row shows positive associations for all regions in both models. The interpersonal row shows positive associations for gray, hippocampal, frontal, and occipital regions in both models, but negative associations for parietal, temporal, ventricular, and log WMH in both models. The resource row shows positive associations for gray, hippocampal, frontal, and occipital regions in both models, but negative associations for parietal, temporal, ventricular, and log WMH in both models.

Conclusions

- Overall, we did not find evidence that early/midlife stressors are associated with brain health in later life.
- Further study of stressor timing, duration, or severity may provide insights into whether associations between the two factors might exist.

Participant demographics

	Total (N=373)	0 stressors (N=302)	≥1 stressor (N=71)
MRI age (Mean (SD))	75.9 (7.4)	75.2 (7.5)	73.8 (7.2)
Stress age (Mean (SD))	34.6 (6.9)	34.8 (7.0)	33.4 (6.3)
Visit interval (yrs) (Mean (SD))	40.3 (3.7)	40.3 (3.6)	40.3 (4.0)
Sex (N (%))			
Female	223 (59.8%)	173 (57.3%)	50 (61.4%)
Male	150 (40.2%)	129 (42.7%)	21 (29.6%)
Education (N (%))			
≤ High school	53 (14.2%)	45 (14.9%)	8 (11.3%)
Some college	138 (37.0%)	104 (34.4%)	34 (47.9%)
≥ College degree	182 (48.8%)	153 (50.7%)	29 (40.8%)
Race & Ethnicity (N (%))			
Asian	58 (15.6%)	52 (17.2%)	6 (8.4%)
Black	165 (44.2%)	125 (41.4%)	40 (56.3%)
Latinx	46 (12.3%)	38 (12.6%)	8 (11.3%)
White	62 (16.6%)	54 (17.9%)	8 (11.3%)
Multiracial/Other group	42 (11.3%)	33 (10.9%)	9 (12.7%)
Study (N (%))			
KHANDLE	226 (60.6%)	189 (62.6%)	32 (45.1%)
STAR	130 (34.9%)	98 (32.4%)	37 (52.1%)
LA90	17 (4.5%)	15 (5.0%)	2 (2.8%)

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STAR

Study of Healthy Aging in African Americans

LIFE After 90

KHANDLESTUDY

Kaiser Healthy Aging and Different Life Experiences