Associations between perceived stress, anxiety, and depressive symptoms with representational similarity in the amygdala's reactivity to negative vs. neutral stimuli in a large adult sample spanning seven decades

Mingtong Liu[1], Kareem I. Al-Khalil[1], Sarah E. Skinner[1], Lauren K. Gresham[1], Elizabeth C. Nord[1], Jinx A. Recchio[1], Stacey M. Schaefer[1]

[1]University of Wisconsin-Madison's Institute on Aging

Research Question: Are perceived stress, anxiety, and depressive symptoms associated with fMRI indices of emotional reactivity to negative vs. neutral stimuli in a large adult sample spanning seven decades?

Background

- Perceived stress has been positively associated with anxiety and depressive symptoms.[1, 2]
- Greater amygdalar reactivity to negative stimuli has been associated with a greater cortisol stress response increase,[3] greater severity of anxiety,[4] and greater severity of depression.[5, 6]
- Understanding how emotional processes in the brain contribute to stress, anxiety, and depressive symptoms in a large adult sample is important for providing insights into the neural basis of mental health and may inform strategies to improve emotional well-being.
- However, previous studies are limited to univariate analyses of amygdalar reactivity and a narrow range of population, therefore this project examines in a large sample with a wide age range

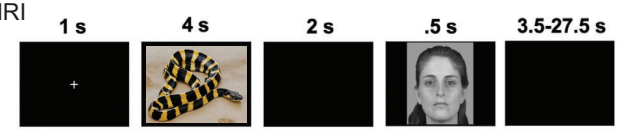
  (1)Associations between amygdalar pattern similarity to negative and neutral images with perceived stress, anxiety, and depressive symptoms.

  (2)Potential mediation pathways between perceived stress, amygdalar pattern similarity to negative and neutral images, anxiety and depressive symptoms.

Methods

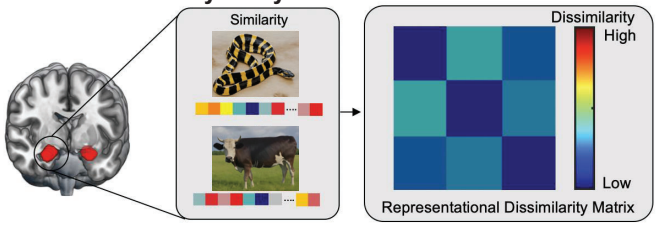
- Participants are from the 3rd follow-up of the Core and 1st assessments within the Refresher samples of the Midlife in the United States (MIDUS) study.
  - N = 259
  - mean age = 57.57 ± 13.47 (SD) years, age range = 26-95
  - 57% female, 30% Black, Indigenous, and/or People of Color
  - 25% with high school or less education, 18% with some college or technical training, and 57% with bachelors or higher degree

Task fMRI



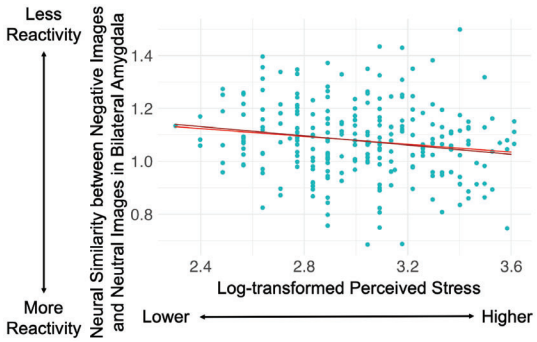
- 90 trials: 30 negative, 30 neutral, 30 positive emotional images (IAPS)[7] paired with a neutral face that followed 2 s after the image

Representational Similarity Analysis



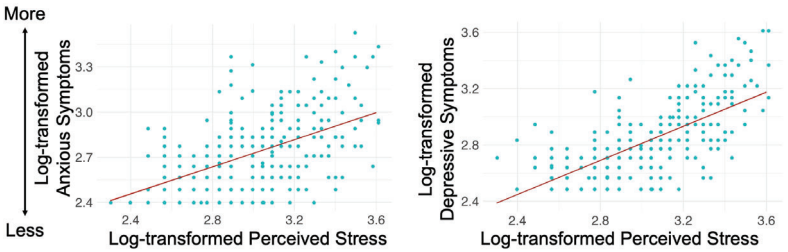
- **Emotional reactivity:** pattern similarity between negative compared to neutral images in the amygdala.

Results



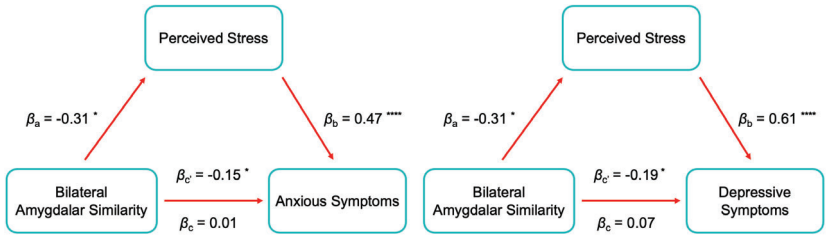
Higher level of perceived stress was significantly related to less bilateral amygdala similarity to negative and neutral images (greater reactivity).

Brown line: Covariates of age, sex, race, education, cohort, and family dependencies adjusted; *Red line:* not adjusted



Higher level of perceived stress was significantly related to more anxiety and depressive symptoms.

No direct associations were found between amygdalar similarity and anxiety, and between amygdalar similarity and depressive symptoms.



Perceived stress mediated the relationships between amygdalar pattern similarity and anxiety, and between amygdalar pattern similarity and depressive symptoms.

Individuals with more amygdalar differentiation between negative and neutral stimuli reported higher perceived stress, which in turn, predicted more anxiety and depressive symptoms.

Conclusions

- Higher level of perceived stress is associated with less bilateral amygdala similarity to negative and neutral stimuli (suggesting greater negative emotional reactivity).
- Amygdalar similarity was not directly associated with levels of anxiety and depressive symptoms.
- Perceived stress indirectly linked amygdalar pattern similarity with both anxiety and depressive symptoms.
- Our findings suggest a greater brain sensitivity to unpleasant events, situations, and experiences in daily lives might contribute vulnerability to anxiety and depression based on stress levels.
- Future directions: Examine whether these relationships are affected by age, sex, racialized identity, or educational attainment.

References & Funding

1. Ezzati, A., Jiang, J., Katz, M.J., Sliwinski, M.J., Zimmerman, M.E., and Lipton, R.B. (2014). Validation of the Perceived Stress Scale in a community sample of older adults. *Int J Geriat Psychiatry* 29, 645–652.
2. Routledge. Sheikh, J.I., and Yesavage, J.A. (2014). Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *In Clinical gerontology* (Routledge), pp. 165–173.
3. Roberts, A.G., Peckins, M.K., Gard, A.M., Hein, T.C., Hardi, F.A., Mitchell, C., Monk, C.S., Hyde, L.W., and Lopez-Duran, N.L. (2022). Amygdala reactivity during socioemotional processing and cortisol reactivity to a psychosocial stressor. *Psychoneuroendocrinology* 144, 105855.
4. Phan, K.L., Fitzgerald, D.A., Nathan, P.J., and Tancer, M.E. (2006). Association between Amygdala Hyperactivity to Harsh Faces and Severity of Social Anxiety in Generalized Social Phobia. *Biological Psychiatry* 59, 424–429.
5. Gaffrey, M.S., Luby, J.L., Belden, A.C., Hirshberg, J.S., Volsch, J., and Barch, D.M. (2011). Association between depression severity and amygdala reactivity during sad face viewing in depressed preschoolers: An fMRI study. *Journal of Affective Disorders* 129, 364–370.
6. Peluso, M.A.M., Glahn, D.C., Matsuo, K., Monkul, E.S., Najt, P., Zamarripa, F., Li, J., Lancaster, J.L., Fox, P.T., Gao, J.-H., et al. (2009). Amygdala hyperactivation in untreated depressed individuals. *Psychiatry Research: Neuroimaging* 173, 158–161.
7. Lang, P.J., Bradley, M.M., and Cuthbert, B.N. (2008). International Affective Picture System (IAPS): Affective ratings of pictures and instruction manual. *Gainesville, FL: University of Florida.*

- Funding: Since 1995, the MIDUS study has been funded by the John D. and Catherine T. MacArthur Foundation Research Network and the National Institute on Aging (P01-AG020166, U19-AG051426, U01-AG077928). The MIDUS Neuroscience Project's data collection was also supported in part by a core grant to the UW-Madison Waisman Center from the National Institute of Child Health and Human Development (P50HD105353).