Effects of Early Life Stress on Brain Networks Supporting Memory During Childhood

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Introduction

• In adults, psychosocial adversity and stress are known to adversely affect memory and its neural substrates (e.g., Conrad, 2010; Roozendaal et al., 2009).
• Developmental research suggests that early life may be a time of heightened susceptibility to environmental stressors (e.g., Tottenham & Sheridan, 2010).
• Prospective, longitudinal studies in humans examining associations between early life stress (ELS), later cognitive abilities, and brain function are limited (cf. Farah et al., 2008).
•The goal of the present study was to examine relations between ELS (i.e., in the first 3-5 years of life) and examine relations with 1) memory ability and 2) hippocampal functional connectivity during childhood.

Methods - Wave 1 (Early Childhood)

Participants

- 175 children (85 male) aged 3-5 years (M= 49.72 ± 9.73 months) participated in the first wave
- Children were recruited based on their mother's history of Major Depressive Disorder (MDD)
  - No Maternal MDD (n=83), Maternal MDD (n=83)

Composite Early Life Stress (ELS) index

- A composite stress index (range: 0-5) was calculated using the following dichotomized environmental adversity variables:
  1) Child exposure to parental depression from birth to Wave 1
  2) Low SES (family income< $40,000/year)
  3) Single-parent household
  4) Neither parent with a college education
  5) High occurrence of major life stressors within the preceding year (≥ 4)

Methods - Wave 2 (Middle Childhood)

Participants

- 91 children (44 female) aged 5-9 years (M= 7.08 ± .83 years) participated in the follow-up memory assessment. Of these, 50 were eligible for scanning. At the time of this report ,35 of these participants had been scanned and yielded useable fMRI data.

Behavioral Assessments

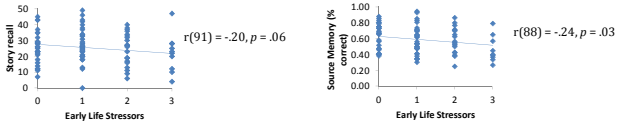
- Episodic memory was assessed using standardized and laboratory-based measures
  1) Story Recall – Children's Memory Scale (CMS)
  2) Objective Source Memory Task
     Children viewed pictures and made 1of 3 semantic judgments (animacy, size, texture). At retrieval children viewed new and old pictures and made both recognition and source memory judgments.

fMRI Assessment

- Hippocampal function was examined via resting-state functional connectivity (rsfc), which allows for the identification of large-scale, functionally-relevant brain networks independent of a task.
  • This technique is particularly useful in developmental populations as the cognitive burden of performing a task while remaining motionless is eliminated (Casey et al., 2005; Uddin et al., 2010).
  • Functional and anatomical data were collected using a 12-channel coil in a Siemen's 3Tesla scanner with standard acquisition parameters.
  • Participants watched a video of abstract patterns/shapes during the 6-minute acquisition of functional data.
  •Functional analyses were conducted using AFNI (Cox, 1996).
  •BOLD signal from white matter and CSF masks and continuous motion regressors from 6 directions (roll, pitch, yaw, x, y, z) were included as noise covariates.
  •Data were band-pass filtered at .005<f<.1.
  •Correlation coefficients were computed between bilateral hippocampal regions of interest and the whole brain using Composite ELS as a covariate.

Results – Memory Performance

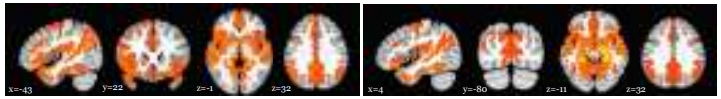
• Greater ELS was modestly related to worse performance on memory tasks.



Results – Hippocampal Functional Connectivity

• Greater ELS was related to greater connectivity between the hippocampus and multiple frontal/prefrontal cortical regions in the left and right hemisphere

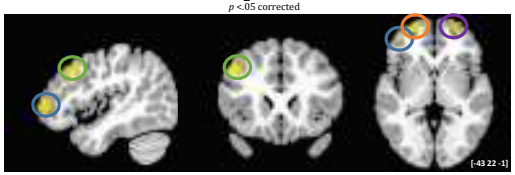
Left Hemisphere Rest **Right Hemisphere Rest**



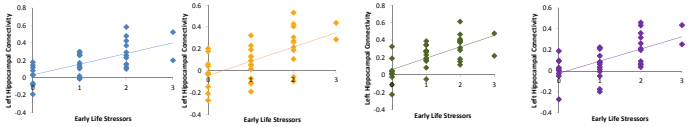
p=7.7x10^{-8} T=6.814

Left Hemisphere & ELS

p <.05 corrected

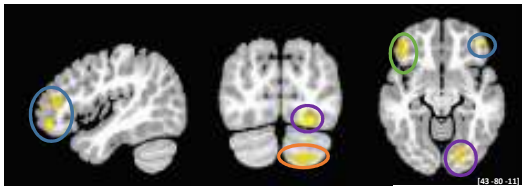


Left Middle Frontal Gyrus (k=103) Left Superior Orbital Gyrus (k=90) Left Middle Frontal Gyrus (k=59) Right Superior Frontal Gyrus (k=45)

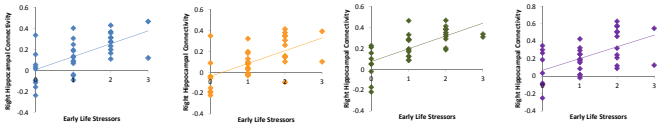


Right Hemisphere & ELS

p <.05 corrected



Right Inferior Frontal Gyrus (k=113) Right Cerebellum (k=61) Left Inferior Frontal Gyrus (k=60) Right Lingual Gyrus (k=45)



Discussion

- These results are consistent with previous research suggesting that exposure to stress results in decreased memory ability.
  - However, they also extend this work by showing relations between early life stress and decreased memory performance in childhood.
- Early life stress was also associated with increased connectivity between the hippocampus and cortical regions.
  - It is possible that this increased connectivity acts as a compensatory mechanism to support memory, thus leading to moderate correlations between ELS and memory.
  - It is also possible that increased connectivity reflects an atypical developmental trajectory, with consequences that will emerge as development continues.
- There were no relations between ELS and hippocampal volume (not shown).
  - This may suggest that alterations to connectivity are detectable first, and that differences in volume emerge overtime.
- Findings from this study add to the body of literature on mechanisms underlying impacts of early life stress later in development.

References

Casey, B., Galvan, A., & Hare, T. A. (2005). Changes in cerebral functional organization during cognitive development. *Current Opinion in Neurobiology, 15(2),* 239–244. doi:10.1016/j.conb.2005.03.012

Conrad, C. D. (2010). A critical review of chronic stress effects on spatial learning and memory. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 34(5),* 742–755. doi:10.1016/j.pnpbp.2009.11.003

Farah, M. J., Betancourt, L., Shera, D. M., Savage, J. H., Giannetta, J. M., Brodsky, N. L., … Hurt, H. (2008). Environmental stimulation, parental nurturance and cognitive development in humans. *Developmental Science, 11(5),* 793–801.

Roozendaal, B., McEwen, B. S., & Chattarji, S. (2009). Stress, memory and the amygdala. *Nature Reviews Neuroscience, 10(6),* 423–433. doi:10.1038/nrn2651

Tottenham, N. & Sheridan, M. (2010). A Review of adversity, the amygdala and the hippocampus: A Consideration of developmental timing. *Frontiers in Human Neuroscience, 3,* 1-18.

Uddin, L. Q., Supekar, K., & Menon, V. (2010). Typical and Atypical Development of Functional Human Brain Networks: Insights from Resting-State fMRI. *Frontiers in Systems Neuroscience, 4.* doi:10.3389/fnsys.2010.00021

Acknowledgements

We would like to thank the families for participating in this study and members of CSEL, NCDL, and the MNC for assistance with subject recruitment and testing, particularly Marisa Tolep, Stephanie Merwin, Katherine Leppert, Lauren Weiss, Jennifer Stark, Alan Siegel, Victoria Smith, and Louis Marti. This research was supported by the University of Maryland (UMD) College of Behavioral and Social Sciences Dean's Research Initiative Award, the UMD Research and Scholars Award, and the National Science Foundation (NSF) in partnership with the University of Maryland ADVANCE Program for Inclusive Excellence Award.

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