Published in final edited form as:

Biol Psychiatry Cogn Neurosci Neuroimaging. 2019 July ; 4(7): 608–609. doi:10.1016/j.bpsc.2019.05.007.

Moving closer to isolating neurocognitive mechanisms of resilience to anxiety in youth with early childhood adversity

Johanna M. Jarcho, Ph.D.

Department of Psychology, Temple University Weiss Hall

Early childhood adversity linked to parenting is associated with increased lifetime risk for numerous mental health disorders [1, 2]. Over the last decade, seminal longitudinal research has demonstrated that lasting effects of these adverse childhood experiences on brain function can diminish or exacerbate this risk [3–5]. In this issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, Callaghan et al. [6] begin to answer a critical question: how do early caregiving experiences “get under the skin” to exert long-term effects on the relation between brain function and symptoms of psychopathology – in this case anxiety. To do so, they build on a well-established rodent literature demonstrating that when exposed to stress in the presence of a parental cue, young pups that have experienced high relative to low quality parenting exhibit diminished behavioral signs of distress, decreased stress hormone release, and blunted amygdala response [7]. Critically, this parental “buffering” effect on amygdala function is absent in older pups [8]. Thus, childhood may be a sensitive period during which the effects of high quality parenting in infancy shapes lasting neurobiological responses to stressors, and whereby the absence of such shaping due to low quality parenting may contribute to heightened amygdala reactivity often associated with anxiety-like behavior. In children, Callaghan et al describe these relations as a neuroenvironmental loop, and hypothesize that early parental care, brain development, and behavior interact to scaffold the maturation of emotion regulation circuitry.

Callaghan et al. [6] made important inroads in testing this hypothesis by pairing neuroimaging with the longitudinal assessment of symptoms of anxiety across 3-years in a unique sample of youth (N=102) who experienced early childhood adversity linked to caregiving (adoption following prior institutionalization; PI), and those who had been reared from birth by their biological parents. During either childhood or adolescence, youth underwent fMRI while viewing photographs of one’s own parent or a stranger. Buffering was defined as a decrease in right amygdala response to viewing one’s own parent relative to a stranger. Overall, children without early childhood adversity exhibited diminished amygdala response, whereas PI children and adolescents from both rearing groups did not. However, a substantial number of youth in both rearing groups exhibited decreased amygdala reactivity. In a test of their neuroenvironmental loop hypothesis, Callaghan et al., then demonstrated that early childhood adversity interacted with brain function to influence the expression of anxiety symptoms across time. Critically, brain function did not relate to

Philadelphia, PA 19122, Phone: 215-204-2616, johanna.jarcho@temple.edu.

Financial Disclosures

Dr. Jarcho has no biomedical financial interests or potential conflicts of interest.

concurrent measures of anxiety, but to changes in anxiety symptoms three years later among PI youth. Specifically, PI youth who exhibited decreased amygdala activity exhibited steeper anxiety reductions across time.

This study has several important implications. The first relates to methodology. The authors utilized information from very early life (PI) to enroll participants into a lagged longitudinal study that enabled the concurrent assessment of children and adolescents across three years that are critical to the expression of anxiety symptoms. The results from this study underscore the fact that information obtained at multiple time points is essential for mapping the complex and temporally protracted relations between early life experience on brain function and subsequent expression of symptoms of psychopathology. Had the authors simply measured relations between early life experience and brain function with concurrent symptoms of anxiety, they would have concluded that amygdala response to parental cues are unrelated to symptoms. Instead, they demonstrated such relations do indeed exist, but for prospective expression of symptoms. Indeed, patterns of neural response that are established in one phase of maturation may have consequences for psychosocial processes that are only engaged later in development as the social milieu increases in complexity. Therefore, a lifespan approach that involves careful selection of the developmentally appropriate age to probe effects of psychosocial experiences and brain function on symptoms of psychopathology is critical to elucidating these nuanced relations.

The second relates to the analytic approach. For analytic purposes, participants were grouped based on information about early life experience (i.e., PI) and demographic features (i.e., age). Although statistically significant effects were obtained using these groupings, a substantial amount of within group heterogeneity in brain response emerged. Given their strong a priori hypotheses regarding brain function, the authors further characterized participants based on whether they demonstrated decreased right amygdala engagement to viewing parents compared to strangers. This mixed method approach of grouping based on early life experience and brain function maps on well to a stress diathesis model of risk for psychopathology. While the early life stress of PI may increase vulnerability to chronic anxiety symptoms, such symptoms may only be sustained in the presence of specific patterns of brain function during critical inflection points in development. This data-driven approach is ideally suited for studies with strong a priori hypotheses about brain function and a sufficient sample size to account for a possible uneven distribution in patterns of functional expression.

The third relates to spurring future research. Numerous interactive effects related to parental care, brain development, and behavior can be tested using a neuroenvironmental loop framework. While Callaghan et al. [6] focused on the lasting effects of adverse parenting in early childhood, growing evidence suggests that the influence of high-quality parenting on brain function can mitigate the expression of psychopathology in at-risk youth [9, 10]. Indeed, Callaghan et al. observed that among PI youth, decreased amygdala reactivity to parents versus strangers was associated with greater feelings of parent-child security. This provides evidence for the hypothesis that high quality parenting is more likely to result in parental buffering. However, alternative explanations warrant exploration. For instance, one might also predict decreased amygdala response for youth who perceive their parent's photo

as more positive and less threatening or novel than a stranger's photo. Thus, a critical next step is to test the effects of parental cues on amygdala response during a stressful situation. This will allow the current findings to be interpreted in the context of the large body of human and non-human research that often characterizes buffering as down-regulation elicited by parental cues during stress.

There is an increasing interest in leveraging fMRI to understand the mechanisms by which risk for psychopathology is instantiated and unfolds across time in youth exposed to adverse childhood events. By demonstrating how neurocognitive mechanisms engaged during sensitive periods in childhood can influence subsequent expression of anxiety symptoms, Callaghan et al. provide an important example of how fMRI can be informative on these mechanisms.

Acknowledgements

This work was supported in part by funds from the NARSAD Young Investigator award: Ellen Schapiro & Gerald Axelbaum Investigator (22441) and grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R21HD093912).

References

1. McLaughlin KA, et al., Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication II: associations with persistence of DSM-IV disorders. *Arch Gen Psychiatry*, 2010 67(2): p. 124–32. [PubMed: 20124112]
2. Green JG, et al., Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry*, 2010 67(2): p. 113–23. [PubMed: 20124111]
3. Green SA, et al., Discrimination of amygdala response predicts future separation anxiety in youth with early deprivation. *J Child Psychol Psychiatry*, 2016 57(10): p. 1135–44. [PubMed: 27260337]
4. Goff B, et al., Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. *Neuroscience*, 2013 249: p. 129–38. [PubMed: 23262241]
5. Almas AN, et al., Effects of early intervention and the moderating effects of brain activity on institutionalized children's social skills at age 8. *Proc Natl Acad Sci U S A*, 2012 109 Suppl 2: p. 17228–31. [PubMed: 23045660]
6. Callaghan BL, et al., Decreased Amygdala Reactivity to Parent Cues Protects Against Anxiety Following Early Adversity: An Examination Across 3 Years. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 2019.
7. Perry RE, Blair C, and Sullivan RM, Neurobiology of infant attachment: attachment despite adversity and parental programming of emotionality. *Curr Opin Psychol*, 2017 17: p. 1–6. [PubMed: 28950954]
8. Sullivan RM and Perry RE, Mechanisms and functional implications of social buffering in infants: Lessons from animal models. *Soc Neurosci*, 2015 10(5): p. 500–11. [PubMed: 26324338]
9. Morgan JK, Shaw DS, and Forbes EE, Maternal depression and warmth during childhood predict age 20 neural response to reward. *J Am Acad Child Adolesc Psychiatry*, 2014 53(1): p. 108–117 e1. [PubMed: 24342390]
10. Guyer AE, et al., Temperament and parenting styles in early childhood differentially influence neural response to peer evaluation in adolescence. *Journal of Abnormal Child Psychology*, 2015 43(5): p. 863–874. [PubMed: 25588884]