

# Moving Closer to Isolating Neurocognitive Mechanisms of Resilience to Anxiety in Youth With Early Childhood Adversity

Johanna M. Jarcho

Early childhood adversity linked to parenting is associated with an 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, the authors focus on anxiety. To do so, they build on established rodent literature demonstrating that when exposed to stress in the presence of a parental cue, young pups that have experienced high-quality parenting 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 shape lasting neurobiological responses to stressors, and whereby the absence of such shaping caused by low-quality parenting may contribute to heightened amygdala reactivity often associated with anxiety-like behavior. In children, Callaghan *et al.* (6) 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 youths ( $n = 102$ ) who experienced early childhood adversity linked to caregiving (adoption after previous institutionalization [PI]) and those who had been reared from birth by their biological parents. During either childhood or adolescence, youths underwent functional magnetic resonance imaging while viewing photographs of their 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 responses, whereas PI children and adolescents from both rearing groups did not. However, a substantial number of youths in both rearing groups exhibited decreased amygdala reactivity. In a test of their neuro-environmental loop hypothesis, Callaghan *et al.* (6) 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 concurrent measures of anxiety but to changes in anxiety symptoms 3 years later among PI youths. Specifically, PI youths who exhibited decreased amygdala activity exhibited steeper anxiety reductions across time.

This study has several important implications. The first relates to methodology. Callaghan *et al.* (6) used information from early life (PI) to enroll participants into a lagged longitudinal study that enabled the concurrent assessment of children and adolescents across 3 years that are often associated with a steep increase in the rates of anxiety symptom expression. 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 the subsequent expression of symptoms of psychopathology. Had Callaghan *et al.* (6) 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 is unrelated to symptoms. Instead, they demonstrated that such relations do indeed exist, but for the 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 (e.g., PI) and demographic features (e.g., 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, Callaghan *et al.* (6) further characterized participants based on whether they demonstrated decreased right amygdala engagement to viewing parents compared with viewing 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

SEE CORRESPONDING ARTICLE ON PAGE 664

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 youths (9,10). Indeed, Callaghan *et al.* (6) observed that among PI youths, 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 youths who perceive their parent's photograph as more positive and less threatening or novel than a photograph of a stranger. 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 nonhuman research that often characterizes buffering as downregulation elicited by parental cues during stress.

There is an increasing interest in leveraging functional magnetic resonance imaging to understand the mechanisms by which risk for psychopathology is instantiated and unfolds across time in youths 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.* (6) provide an important example of how functional magnetic resonance imaging can be informative on these mechanisms.

### Acknowledgments and Disclosures

This work was supported by the National Alliance for Research on Schizophrenia and Depression Young Investigator Award: Ellen Schapiro and Gerald Axelbaum Investigator (No. 22441) and by Eunice Kennedy Shriver National Institute of Child Health and Human Development Grant No. R21HD093912.

The author reports no biomedical financial interests or potential conflicts of interest.

### Article Information

From the Department of Psychology, Temple University, Philadelphia, Pennsylvania.

Address correspondence to Johanna M. Jarcho, Ph.D., Department of Psychology, Temple University, Weiss Hall 866, 1701 N 13th St., Philadelphia, PA 19122; E-mail: [johanna.jarcho@temple.edu](mailto:johanna.jarcho@temple.edu).

Received May 13, 2019; accepted May 16, 2019.

### References

- McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2010): Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication II: Associations with persistence of DSM-IV disorders. *Arch Gen Psychiatry* 67:124–132.
- Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2010): Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: Associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry* 67:113–123.
- Green SA, Goff B, Gee DG, Gabard-Durnam L, Flannery J, Telzer EH, *et al.* (2016): Discrimination of amygdala response predicts future separation anxiety in youth with early deprivation. *J Child Psychol Psychiatry* 57:1135–1144.
- Goff B, Gee DG, Telzer EH, Humphreys KL, Gabard-Durnam L, Flannery J, Tottenham N (2013): Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. *Neuroscience* 249:129–138.
- Almas AN, Degnan KA, Radulescu A, Nelson CA 3rd, Zeanah CH, Fox NA (2012): 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* 109(suppl 2):17228–17231.
- Callaghan BL, Gee DG, Gabard-Durnam L, Telzer EH, Humphreys KL, Goff B, *et al.* (2019): Decreased amygdala reactivity to parent cues protects against anxiety following early adversity: An examination across 3 years. *Biol Psychiatry Cogn Neurosci Neuroimaging* 4:664–671.
- Perry RE, Blair C, Sullivan RM (2017): Neurobiology of infant attachment: Attachment despite adversity and parental programming of emotionality. *Curr Opin Psychol* 17:1–6.
- Sullivan RM, Perry RE (2015): Mechanisms and functional implications of social buffering in infants: Lessons from animal models. *Soc Neurosci* 10:500–511.
- Morgan JK, Shaw DS, Forbes EE (2014): Maternal depression and warmth during childhood predict age 20 neural response to reward. *J Am Acad Child Adolesc Psychiatry* 53:108–117e1.
- Guyer AE, Jarcho JM, Pérez-Edgar K, Degnan KA, Pine DS, Fox NA, Nelson EE (2015): Temperament and parenting styles in early childhood differentially influence neural response to peer evaluation in adolescence. *J Abnorm Child Psychol* 43:863–874.