Title

Adolescent Psychopathology: The Role of Brain-Based Diatheses, Sensitivities, and Susceptibilities

Journal

Child Development Perspectives, 14(2)

ISSN

1750-8592

Author

Guyer, Amanda E

Publication Date

2020-06-01

DOI

10.1111/cdep.12365

Peer reviewed

HHS Public Access

Author manuscript

Child Dev Perspect. Author manuscript; available in PMC 2021 June 01.

Published in final edited form as:

Child Dev Perspect. 2020 June ; 14(2): 104–109. doi:10.1111/cdep.12365.

Adolescent Psychopathology: The Role of Brain-based Diatheses, Sensitivities, and Susceptibilities

Amanda E. Guyer

University of California, Davis

Abstract

The rates of onset for several forms of psychopathology peak during adolescence, which coincides with the refinement of brain circuitry attuned to expanding social-contextual interactions, stressors, and settings. While some adolescents experience mental health difficulties, most do not develop significant problems. Conceptual work suggests that brain-based individual differences in adolescents' neurobiological susceptibility to their social contexts play a role in the development of psychopathology and well-being. In this article, I summarize evidence supporting the idea that individual differences in brain structure and function moderate the relation between adolescents' social-contextual experiences and psychopathology. I discuss why this approach is important in developmental research designed to identify adolescents at greatest risk for psychopathology or poised for positive outcomes, as well as those who may benefit most from intervention.

Keywords

adolescence; brain development; mental health

The word *adolescent* frequently conjures up images of young people who are moody, sullen, taking drugs, fighting, or driving recklessly. Some aspects of this depiction reflect the fact that rates of affective disorders, substance use, and conduct problems are markedly higher during adolescence than before the onset of puberty. Yet many young people traverse this transitional period of development without considerable problems. Why do some adolescents sail through without significant behavioral or emotional difficulties or even thrive, whereas others experience debilitating impairment?

Developmental scientists have long recognized that development is a complex interplay of individuals' biology and the environments in which they are situated. In this article, I describe conceptual frameworks used to understand individual differences in children's and adolescents' biological vulnerability or susceptibility to their environments. Then I present findings from studies designed to identify at-risk adolescents based on variability in brain structure and function. By discovering neurophysiological factors sensitive to contextual variations and demonstrating how these in concert predict adjustment, we can generate new information about brain-based mechanisms of adolescent psychopathology and well-being,

Corresponding author: Amanda E. Guyer, Ph.D., Department of Human Ecology, Center for Mind and Brain, University of California Davis, 267 Cousteau Place, Davis, CA 95618, aeguyer@ucdavis.edu.

clarify the generalizability of these processes across individuals, and improve identification of and support for adolescents at risk for psychopathology.

Biology x Environment Models of Development

Foundational research on risk for psychopathology has used the *diathesis stress model* to explain its emergence (Meehl, 1962; Monroe & Simons, 1991). This model assumes that interactions between a diathesis (an inherent, biologically based vulnerability) and environmental stressors set the stage for psychopathology to develop. Psychopathology is more likely to emerge if an individual both possesses the vulnerability (e.g., a genotype, negative temperament) and experiences a negative environment (e.g., abusive parents, stressful life events); without exposure to the negative environment, the vulnerability would likely remain dormant (Rutter & Silberg, 2002). Although some gene (e.g., serotonin transporter) x environment effects have not replicated (Culverhouse et al., 2018), diathesis stress is evident across a range of psychopathologies, including depression (Gazelle & Ladd, 2003; Hankin, 2008), antisocial behavior (Cicchetti, Rogosch, & Thibodeau, 2012), internalizing problems (Hastings et al., 2015), and externalizing problems (Schermerhorn et al., 2013), illustrating one reason why some youth with certain vulnerabilities develop psychopathology and others do not.

Another set of theories, *differential susceptibility* (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007; Belsky & Pluess, 2009) and *biological sensitivity to context* (Boyce & Ellis, 2005), integrated as *neurobiological susceptibility to the environment* (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011), stipulates that some individuals are more or less susceptible or sensitive to their environments through genetic, temperament, and physiological reactivity factors instantiated by central nervous system processes. Highly susceptible or sensitive individuals do poorly in stressful or difficult environments, but do well in supportive or positive environments; less susceptible or sensitive individuals are less influenced by the environment, whether positive or negative. Unlike the diathesis stress focus on negative outcomes from vulnerability to adversity, these perspectives emphasize plasticity to bivalent environments and outcomes. Several factors related to susceptibility and sensitivity have been reported, including candidate genes (Bakermans-Kranenburg & Van IJzendoorn, 2011), polygenic risk (a measure that predicts a trait based on multiple genetic variations and indicates how a person's risk compares to others with a different genetic makeup; Shaw et al., 2019), high stress reactivity (Obradović, Bush, Stamperdahl, Adler, & Boyce, 2010), and temperament (Slagt, Dubas, Deković, & van Aken, 2016).

One framework of adolescent development (Schriber & Guyer, 2016) suggests that tests of diathesis stress, biological sensitivity to context, or differential susceptibility include measures of brain function and structure because research guided by these models has included early-life markers of temperament, genetic variation, and stress reactivity, but not direct brain indices. Although individual differences in neurobiological susceptibility to social context can occur at any age or developmental phase, adolescence may be a particularly pivotal time to examine interactive effects of the brain because it is a period of significant brain development (second to infancy), heightened sensitivity to social contexts, and increased onset of psychopathology (Schriber & Guyer, 2016). Susceptibility is rooted

in neurobiology, and both genetic processes and one's experiences shape brain development, all of which contribute to individual differences in neurobiological susceptibility (Ellis et al., 2011). This suggests that brain metrics measured in adolescence may be less of a true diathesis (i.e., not an inherent predisposition) and more of a susceptibility or sensitivity factor given environmental influences on the brain leading to adolescence. Also, certain brain characteristics could be diatheses once they reach a more developed state, whether in infancy or adolescence. While this hypothesis needs to be tested empirically, it has implications for the age at which researchers collect data on the brain, the regions to focus on (e.g., earlier- or later-developing ones, such as the amygdala or prefrontal cortex [PFC]), and neurodevelopmental processes (e.g., cortical thinning) when testing diatheses, susceptibilities, or sensitivities.

Magnetic resonance imaging (MRI), electroencephalogram (EEG), and near-infrared spectrometry techniques allow us to measure different brain indices, such as regional volumes, cortical thinning, and responses to stimuli. Certain brain regions have been of particular interest because of their involvement in negative affect (i.e., the amygdala and the anterior cingulate cortex [ACC]), self-regulation (PFC), and sensitivity to stressors (hippocampus), but also because research has linked these regions to psychopathologies like depression and conduct problems. Thus, considering adolescent brain structure and function markers of diatheses, sensitivities, or susceptibilities can provide a mechanistic understanding of (mal)adjustment. Next, I discuss research related to the adolescent neurobiological susceptibility to social context framework (advanced in Schriber & Guyer, 2016) by considering brain indices as diathesis, sensitivity, or susceptibility factors. I describe neuroimaging studies that tested moderating effects of individual differences in adolescents' brain structure, and then brain function, in concert with stressful or supportive social-contextual experiences to identify adolescents at more or less risk for psychopathology. I conclude with questions and next steps for research.

Brain Structure

Measuring characteristics of adolescent brain structure (e.g., gray matter volume, cortical thinning) has revealed how some environmental influences relate to psychopathology. Three studies provide evidence for anatomical markers of adolescents' brain-based susceptibility to context in relation to depression (Schriber et al., 2017; Whittle et al., 2011; Yap et al., 2008). In two of the studies, the context was a challenging conflict-resolution discussion between adolescents and their mothers. Boys with larger amygdala volumes and a smaller left than right ACC volume had the lowest levels of depression when their mothers showed low levels of aggression during the discussion (Yap et al., 2008). However, girls with a smaller amygdala volume had the lowest levels of depression if their mothers were also low in aggressiveness during the interaction, but the highest levels of depression if their mothers were high in aggressiveness. In addition, girls with larger hippocampi exhibited greater and lesser change in symptoms of depression from early to midadolescence when their mothers were high or low in aggressiveness, respectively, during the discussion (Whittle et al., 2011). These moderation effects revealed that a smaller amygdala volume but larger hippocampal volume might render girls more susceptible than boys to both positive and negative parenting climates. Whereas boys showed a general neural sensitivity to parenting quality,

girls appeared to reap the benefits of more supportive interactions with their mothers but endure the consequences of harsher interactions as a function of amygdala and hippocampus volume. These results reveal sex differences in heightened susceptibility to psychosocial dynamics in the home, indicate possible contributing factors to the greater incidence of depression in girls than boys in adolescence (Breslau et al., 2017), and highlight the need to test sex differences in work of this type for other psychopathologies.

Extending prior research (Whittle et al., 2011), and as specified by adolescent neurobiological susceptibility to social context (Schriber & Guyer, 2016), another of the studies examined hippocampal volume as a moderator of the effects of advantageous (i.e., family connectedness) and adverse (i.e., exposure to crime in the community) adolescent-relevant social contexts on adolescents' symptoms of depression (Schriber et al., 2017). The study examined relations in Mexican-origin adolescents living in predominantly lower-income homes. Thus, risk and protective factors varied for these youth, who were likely to be exposed to crime but also to be connected to family (also termed *familism*, a Latino value grounded in family loyalty and cohesiveness). Moderation effects indicated that family connection and exposure to community crime predicted symptoms of depression differentially depending on adolescents' hippocampal volume (regardless of sex). Adolescents with larger hippocampal volumes reported more severe levels of depressive symptoms when they felt less connected to their family or experienced more community crime, but less severe symptoms when they felt more connected to family or had low exposure to crime. Adolescents with smaller hippocampal volumes were not susceptible to divergent degrees of family connection or community exposure to crime in relation to symptoms. Thus, in adolescents with larger hippocampi, feeling relatively disconnected from one's family or having high exposure to crime may increase the likelihood of risk for depression, whereas feeling closely connected to one's family or having low exposure to crime may reduce that risk. Collectively, in these studies, hippocampal volume in adolescence was a marker of openness to the effects of both positive and negative social contexts on risk for depression (Schriber et al., 2017; Whittle et al., 2011).

These studies measured brain anatomy at just one point, yet significant changes in brain development occur across adolescence. One such change is greater cortical thinning of the PFC, with less thinning a marker of delayed brain development. A recent study examined cortical thinning over time as a moderator of positive and negative social-contextual influences on negative (depressive symptoms) and positive (well-being) outcomes (Deane et al., 2019). The study accounted for within-person change in brain anatomy because measuring a snapshot at one time is insufficient for identifying susceptibilities in all youth at a given age since brain development progresses at different paces for different youth. The results suggested differential susceptibility effects whereby PFC development interacted with aggressive parenting behaviors in predicting adolescents' subsequent well-being but not symptoms of depression. For adolescents with reduced cortical thinning, well-being was compromised when their mothers acted more aggressively toward them but enhanced when their mothers acted less aggressively. Although genetics and environment influence the cortex in different ways across development (Lenroot et al., 2009), experience-dependent processes modify cortical thinning in adolescence and may signify susceptibility to social context, not diathesis stress, as seen in this study.

Brain Function

Another individual characteristic that may indicate diathesis stress or susceptibility to social context in adolescence is brain function. A common way to measure brain function with MRI or EEG is to use experimental tasks with conditions designed to elicit responses from specific brain regions to different kinds of stimuli (e.g., words, pictures). Measuring brain responses to different stimuli may reveal subtle components of behaviors, cognitions, and emotions, particularly for processes with manifestations less evident through self-reports or observations (e.g., rapid emotional reactivity). Evidence from neuroimaging work in adolescents, coupled with evidence from studies of adults (Gard, Shaw, Forbes, & Hyde, 2018) and EEG methods (Goldstein et al., 2019), support the idea that individual variability in the brain's responsivity to specific environmental cues creates a dependency for the way in which social-contextual factors influence psychopathology.

Adolescent brain function was examined as a moderator of social context in the study of Mexican-origin youth described earlier. In a pattern consistent with diathesis stress, the link between adolescents' exposure to crime in their community and conduct problems depended on their level of brain activity when thinking about how another person's emotional cues made them feel, referred to as *emotion introspection* (Weissman et al., 2018). Emotion introspection involves representing one's own or others' mental states and emotions, and continued exposure to community violence might make adolescents less sensitive to others' displays of emotional distress (Mrug, Madan, & Windle, 2016). For adolescents with reduced activity in the posterior cingulate cortex, temporoparietal junction, and amygdala during emotion introspection, conduct problems were especially elevated in the context of high but not low levels of exposure to crime. For adolescents with high activity in these regions, conduct problems were similar regardless of the degree of exposure to crime. Adolescents living in high-crime communities with these patterns of neural activity may be more vulnerable to mirroring aggressive or harmful activities around them because they might have reduced capacity for representing others' feelings or processing others' distress cues as salient. Earlier exposure to crime or concomitant factors may have influenced adolescents' brain activity, limiting its classification as a true diathesis and highlighting the need to consider developmental history. Nonetheless, demonstrating moderation by brain activity in these regions, known for their role in the perception, interpretation, and reflection of others' emotions, advances explanations for why some youth develop conduct problems in the context of exposure to crime. Interventions to reduce conduct problems for youth living in high-crime areas could target components of emotion introspection about others' distress.

Brain reactivity to social exclusion has also been tested in the link between Mexican-origin adolescents' experiences of hostile environments and deviant behavior (Schriber et al., 2018). Here, the focus was on subgenual ACC because this region is highly reactive to being socially excluded (Masten et al., 2011). A moderation effect indicated that adolescents with the highest levels of subgenual ACC reactivity to social exclusion who felt relatively disconnected from their families had the highest levels of deviant behavior, but those with the lowest levels of subgenual ACC who felt disconnected had the lowest levels of deviant behavior. Similarly, in another study, adolescents with high caudate activation in response to

parental praise who also reported feeling unaccepted by their mothers showed the strongest positive association between peer victimization and symptoms of depression (Sequeira, Butterfield, Silk, Forbes, & Ladouceur, 2019). Caudate activity relates to reward prediction errors and in this case, adolescents with high activity may not have expected to hear positive praise, possibly because they had a history of infrequent positive social feedback from their mothers or peers.

These studies demonstrate that the brain's reactivity to social threats or reward cues renders adolescents more sensitive or susceptible to characteristics of their family relationships, which in turn results in less optimal outcomes given negative social contexts of feeling disconnected to or unaccepted by family. For youth in difficult family contexts, interventions may help by shifting their attention to and perception of social cues. In these studies, neurobiological susceptibility to social context effects were seen for both deviant behavior and depression, although they involved different brain regions and social contexts, raising questions about domain-general or domain-specific influences. Overall, these findings illuminate who is at heightened risk for psychopathology given both the social contexts they have experienced and the functioning of different brain regions through which the risk operates.

Conclusions

What is the added value of testing brain indices as markers of diathesis stress and neurobiological susceptibility to social context? I return to this article's guiding question: Why, despite challenging experiences, do some children do well while others flounder? As illustrated by the studies I have reviewed, accounting for indices of brain structure and function facilitated consideration of if, when, how, and the degree to which adolescents' social experiences depend on individual brain characteristics in influencing their adjustment. Specifically, although suboptimal behavior could change through intervention without knowledge of the brain's role, determining brain-based diathesis or susceptibility factors is helpful in identifying youth at high risk for psychopathology. This can be done based on the behaviors and psychological processes supported by the brain region or function examined, including subtle aspects of cognition and emotion difficult to measure through self-reports or observations. Including direct measures of the brain's structure and processing of social cues also reveals specific social contexts as more or less influential on adolescent psychopathology, contexts that may otherwise go undetected. This complex perspective warrants further consideration in broader outlets, and I encourage researchers and others to conceptually and methodologically advance the propositions raised because the evidence base is just beginning to build.

Adolescent brain reactivity to stimuli changes through intervention (Forbes et al., 2010; Maslowsky et al., 2010). Thus, identifying relevant, modifiable brain markers may provide new clues about what social-contextual input can help adolescents manage their thoughts and emotions more effectively. If we can determine which brain circuits are more or less indicative of openness to the influence of which contexts, we may be able to develop new interventions or therapies. PFC reactivity may be more susceptible to peer contexts than parent contexts, and amygdala reactivity may be more susceptible to parent contexts than

peer contexts. Interventions could be designed to pair PFC-based functions within peer contexts to address conduct problems and amygdala-based functions within parent contexts to address depression. Moreover, because some social-contextual risk factors can be modified, identifying specific social processes and their role in brain x environment effects can inform the design of interventions for at-risk adolescents to alter their outcomes through the social processes and contexts (e.g., parenting, peer affiliations, community crime) most relevant to their age and ethnicity. How adolescents process the information around them (e.g., risks, rewards, consequences, others' emotions), and use it to regulate their emotions and behaviors, is based partially on the values instilled through their culture and family, as well as on their social interactions leading to adolescence and through the transition to adulthood.

Research on brain-based diathesis and susceptibility factors should incorporate different tasks and social contexts, both beneficial and detrimental, that are relevant to adolescents (e.g., school); additional brain-based characteristics (e.g., functional connectivity); developmental history; and positive outcomes as well as other forms of psychopathology (e.g., anxiety). For example, the studies I have reviewed primarily linked brain structure with depression and brain function with conduct problems; each index should be examined for other types of psychopathology. Some psychopathologies may be more or less influenced by neurobiological susceptibility than others. Furthermore, research needs to characterize within-person changes in brain structure and function to determine the degree to which brain reactivity or anatomy markers are a function of maturation or learning effects, and which are trait or state in nature (Guyer, Pérez-Edgar, & Crone, 2018). Important questions also remain about whether adolescent neurobiological susceptibility to context is synonymous with biologically based vulnerability (as in diathesis stress) or an acquired susceptibility that emerges from adverse experiences. Some brain susceptibilities may operate in tandem with other biological metrics of sensitivity to context. These distinctions may further depend on the brain region for a given psychopathological outcome or environmental influence.

Finally, reliability, validity, and standardization of neuroimaging tasks and analytic approaches is needed to maintain consistency across findings and aid in their interpretation and replication. In the seven studies I reviewed in this article, the magnitude of effects differed by brain region and type of social-contextual variable (e.g., family connectedness versus crime exposure), but three studies found effects considered medium in magnitude by standard effect size conventions, three found small effects, and one found an effect considered large. Tests of the theoretical predictions should also be applied to understand the valence and range of environmental influence and variance of individual differences. Upon identifying a significant moderation effect, researchers typically differentiate diathesis stress and differential susceptibility models by visual inspection of interaction plots created from simple slopes analyses. If both models show the same slopes, then the location of where the regression lines cross (or not), the crossover point, becomes an important distinction between models. Some researchers recommend interpreting results from the competing models using the magnitude of the *F*-ratio for the interaction (rather than significance testing) and calculating the crossover point (Belsky & Widaman, 2018; Widaman et al., 2012). Indices have been developed (Roisman et al., 2012) to distinguish between diathesis stress and differential susceptibility evidence: the regions of significance on the independent

variable (X), meaning the values at which the moderator and outcome are correlated, bounded by a conventional range of +/−2SD from X's mean; proportion of the interaction showing a more or less optimal outcome; and proportion of individuals affected differentially by the moderator. Applying these guidelines will help discern diathesis stress from differential susceptibility effects on adolescent outcomes, as a function of brain-based moderators.

Research on adolescent neurobiological susceptibility to social context can inform theory about how aspects of the brain and environment create risk for psychopathology or opportunity for well-being. We need to disseminate findings about how neurobiology operates in concert with social contexts to educators, policymakers, and practitioners working in public health, education, criminal justice, and mental health. A challenge for families, clinicians, and communities is to find ways to support youth with brain-based context diatheses, sensitivities, or susceptibilities, for better or worse, such as helping them reign in aggressiveness in interpersonal exchanges, interpret others' emotional cues, or cultivate feelings of family connection.

Acknowledgments:

This work was supported by a William T. Grant Foundation Scholars Award (#180021) and National Institutes of Health grants R01MH098370 and R03MH116519. The author would like to thank Koraly Perez-Edgar, Paul Hastings, Grant Shields, and Joseph Venticinque for their feedback.

References

Bakermans-Kranenburg MJ, & Van IJzendoorn MH (2011). Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. Development and Psychopathology, 23, 39–52. .10.1017/S0954579410000635 [PubMed: 21262038]

Belsky J, Bakermans-Kranenburg MJ, & Van IJzendoorn MH (2007). For better and for worse: Differential susceptibility to environmental influences. Current Directions in Psychological Science, 16, 300–304. 10.1111/j.1467-8721.2007.00525.x

Belsky J, & Pluess M (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. Psychological Bulletin, 135, 885–908. 10.1037/a0017376 [PubMed: 19883141]

Belsky J, & Widaman K (2018). Editorial perspective: Integrating exploratory and competitive–confirmatory approaches to testing person × environment interactions. Journal of Child Psychology and Psychiatry and Allied Disciplines, 59, 296–298. 10.1111/jcpp.12824

Boyce WT, & Ellis BJ (2005). Biological sensitivity to context: I. An evolutionary-developmental theory of the origins and functions of stress reactivity. Development and Psychopathology, 17, 271–301. 10.1017/S0954579405050145 [PubMed: 16761546]

Breslau J, Gilman SE, Stein BD, Ruder T, Gmelin T, & Miller E (2017). Sex differences in recent first-onset depression in an epidemiological sample of adolescents. Translational Psychiatry, 7, e1139 10.1038/tp.2017.105 [PubMed: 28556831]

Cicchetti D, Rogosch FA, & Thibodeau EL (2012). The effects of child maltreatment on early signs of antisocial behavior: Genetic moderation by tryptophan hydroxylase, serotonin transporter, and monoamine oxidase A genes. Development and Psychopathology, 24, 907–928. 10.1017/S0954579412000442 [PubMed: 22781862]

Culverhouse RC, Saccone NL, Horton AC, Ma Y, Anstey KJ, Banaschewski T, … Bierut LJ (2018). Collaborative meta-analysis finds no evidence of a strong interaction between stress and 5-HTTLPR genotype contributing to the development of depression. Molecular Psychiatry, 23, 133–142. 10.1038/mp.2017.44 [PubMed: 28373689]

Deane C, Vijayakumar N, Allen NB, Schwartz O, Simmons JG, Bousman CA, … Whittle S (2019). Parenting × brain development interactions as predictors of adolescent depressive symptoms and well-being: Differential susceptibility or diathesis-stress? Development and Psychopathology, 32, 139–150. 10.1017/s0954579418001475

Ellis BJ, Boyce WT, Belsky J, Bakermans-Kranenburg MJ, & van IJzendoorn MH (2011). Differential susceptibility to the environment: An evolutionary-neurodevelopmental theory. Development and Psychopathology, 23, 7–28. 10.1017/S0954579410000611 [PubMed: 21262036]

Forbes EE, Olino TM, Ryan ND, Birmaher B, Axelson D, Moyles DL, & Dahl RE (2010). Reward-related brain function as a predictor of treatment response in adolescents with major depressive disorder. Cognitive, Affective and Behavioral Neuroscience, 10, 107–118. 10.3758/CABN.10.1.107

Gard AM, Shaw DS, Forbes EE, & Hyde LW (2018). Amygdala reactivity as a marker of differential susceptibility to socioeconomic resources during early adulthood. Developmental Psychology, 54, 2341–2355. 10.1037/dev0000600 [PubMed: 30359060]

Gazelle H, & Ladd GW (2003). Anxious solitude and peer exclusion: A diathesis-stress model of internalizing trajectories in childhood. Child Development, 74, 257–278. 10.1111/1467-8624.00534 [PubMed: 12625449]

Goldstein BL, Kessel EM, Kujawa A, Finsaas MC, Davila J, Hajcak G, & Klein DN (2019). Stressful life events moderate the effect of neural reward responsiveness in childhood on depressive symptoms in adolescence. Psychological Medicine, 1–8. 10.1017/S0033291719001557

Guyer AE, Pérez-Edgar K, & Crone EA (2018). Opportunities for neurodevelopmental plasticity from infancy through early adulthood. Child Development, 89, 687–697. 10.1111/cdev.13073 [PubMed: 29664997]

Hankin BL (2008). Cognitive vulnerability-stress model of depression during adolescence: Investigating depressive symptom specificity in a multi-wave prospective study. Journal of Abnormal Child Psychology, 36, 999–1014. 10.1007/s10802-008-9228-6 [PubMed: 18437551]

Hastings PD, Helm J, Mills RSL, Serbin LA, Stack DM, & Schwartzman AE (2015). Dispositional and environmental predictors of the development of internalizing problems in childhood: Testing a multilevel model. Journal of Abnormal Child Psychology, 43, 831–845. 10.1007/s10802-014-9951-0 [PubMed: 25411124]

Lenroot RK, Schmitt JE, Ordaz SJ, Wallace GL, Neale MC, Lerch JP, … Giedd JN (2009). Differences in genetic and environmental influences on the human cerebral cortex associated with development during childhood and adolescence. Human Brain Mapping, 30, 163–174. 10.1002/hbm.20494 [PubMed: 18041741]

Maslowsky J, Mogg K, Bradley BP, McClure-Tone E, Ernst M, Pine DS, & Monk CS (2010). A preliminary investigation of neural correlates of treatment in adolescents with generalized anxiety disorder. Journal of Child and Adolescent Psychopharmacology, 20, 105–111. 10.1089/cap.2009.0049 [PubMed: 20415605]

Masten CL, Eisenberger NI, Borofsky LA, McNealy K, Pfeifer JH, & Dapretto M (2011). Subgenual anterior cingulate responses to peer rejection: A marker of adolescents' risk for depression. Development and Psychopathology, 23, 283–292. 10.1017/S0954579410000799 [PubMed: 21262054]

Meehl PE (1962). Schizotaxia, schizotypy, schizophrenia. American Psychologist, 17, 827–838. 10.1037/h0041029

Monroe SM, & Simons AD (1991). Diathesis-stress theories in the context of life stress research: Implications for the depressive disorders. Psychological Bulletin, 110, 406–425. 10.1037/0033-2909.110.3.406 [PubMed: 1758917]

Mrug S, Madan A, & Windle M (2016). Emotional desensitization to violence contributes to adolescents' violent behavior. Journal of Abnormal Child Psychology, 44, 75–86. 10.1007/s10802-015-9986-x [PubMed: 25684447]

Obradović J, Bush NR, Stamperdahl J, Adler NE, & Boyce WT (2010). Biological sensitivity to context: The interactive effects of stress reactivity and family adversity on socioemotional behavior and school readiness. Child Development, 81, 270–289. 10.1111/j.1467-8624.2009.01394.x [PubMed: 20331667]

Roisman GI, Newman DA, Fraley RC, Haltigan JD, Groh AM, & Haydon KC (2012). Distinguishing differential susceptibility from diathesis-stress: Recommendations for evaluating interaction effects. Development and Psychopathology, 24, 389–409. 10.1017/S0954579412000065 [PubMed: 22559121]

Rutter M, & Silberg J (2002). Gene-environment interplay in relation to emotional and behavioral disturbance. Annual Review of Psychology, 53, 463–490. 10.1146/annurev.psych.53.100901.135223

Schermerhorn AC, Bates JE, Goodnight JA, Lansford JE, Dodge KA, & Pettit GS (2013). Temperament moderates associations between exposure to stress and children's externalizing problems. Child Development, 84, 1579–1593. 10.1111/cdev.12076 [PubMed: 23438634]

Schriber RA, Anbari Z, Robins RW, Conger RD, Hastings PD, & Guyer AE (2017). Hippocampal volume as an amplifier of the effect of social context on adolescent depression. Clinical Psychological Science, 5, 632–649. 10.1177/2167702617699277 [PubMed: 28740744]

Schriber RA, & Guyer AE (2016). Adolescent neurobiological susceptibility to social context. Developmental Cognitive Neuroscience, 19, 1–18. 10.1016/j.dcn.2015.12.009 [PubMed: 26773514]

Schriber RA, Rogers CR, Ferrer E, Conger RD, Robins RW, Hastings PD, & Guyer AE (2018). Do hostile school environments promote social deviance by shaping neural responses to social exclusion? Journal of Research on Adolescence, 28, 103–120. 10.1111/jora.12340 [PubMed: 29460355]

Sequeira SL, Butterfield RD, Silk JS, Forbes EE, & Ladouceur CD (2019). Neural activation to parental praise interacts with social context to predict adolescent depressive symptoms. Frontiers in Behavioral Neuroscience, 13, 1–15. 10.3389/fnbeh.2019.00222 [PubMed: 30697155]

Shaw DS, Galán CA, Lemery-Chalfant K, Dishion TJ, Elam KK, Wilson MN, & Gardner F (2019). Trajectories and predictors of children's early-starting conduct problems: Child, family, genetic, and intervention effects. Development and Psychopathology, 31, 1911–1921. 10.1017/S0954579419000828 [PubMed: 31370912]

Slagt M, Dubas JS, Deković M, & van Aken MAG (2016). Differences in sensitivity to parenting depending on child temperament: A meta-analysis. Psychological Bulletin, 142, 1068–1110. 10.1037/bul0000061 [PubMed: 27513919]

Weissman DG, Gelardi KL, Conger RD, Robins RW, Hastings PD, & Guyer AE (2018). Adolescent externalizing problems: Contributions of community crime exposure and neural function during emotion introspection in Mexican-origin youth. Journal of Research on Adolescence, 28, 551–563. 10.1111/jora.12358 [PubMed: 29080233]

Whittle S, Yap MBH, Sheeber L, Dudgeon P, Yücel M, Pantelis C, … Allen NB (2011). Hippocampal volume and sensitivity to maternal aggressive behavior: A prospective study of adolescent depressive symptoms. Development and Psychopathology, 23, 115–129. 10.1017/s0954579410000684 [PubMed: 21262043]

Widaman KF, Helm JL, Castro-Schilo L, Pluess M, Stallings MC, & Belsky J (2012). Distinguishing ordinal and disordinal interactions. Psychological Methods, 17, 615–622. 10.1037/a0030003 [PubMed: 22984788]

Yap MBH, Whittle S, Yücel M, Sheeber L, Pantelis C, Simmons JG, & Allen NB (2008). Interaction of parenting experiences and brain structure in the prediction of depressive symptoms in adolescents. Archives of General Psychiatry, 65, 1377–1385. 10.1001/archpsyc.65.12.1377 [PubMed: 19047524]