Published in final edited form as:

Biol Psychiatry Cogn Neurosci Neuroimaging. 2021 February ; 6(2): 188–199. doi:10.1016/j.bpsc.2020.07.020.

A Social Affective Neuroscience Model of Risk and Resilience in Adolescent Depression: Preliminary Evidence and Application to Sexual and Gender Minority Adolescents

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Abstract

Depression is a disorder of dysregulated affective and social functioning, with attenuated response to reward, heightened response to threat (perhaps especially social threat), excessive focus on negative aspects of the self, ineffective engagement with other people, and difficulty modulating all of these responses. Known risk factors provide a starting point for a model of developmental pathways to resilience, and we propose that the interplay of social threat experiences and neural social-affective systems is critical to those pathways. We describe a model of risk and resilience, review supporting evidence, and apply the model to sexual and gender minority adolescents, a population with high disparities in depression and unique social risk factors. This approach illustrates the fundamental role of a socially and developmental informed clinical neuroscience model for understanding a population disproportionately affected by risk factors and psychopathology outcomes. We consider it a public health imperative to apply conceptual models to high-need populations to elucidate targets for effective interventions to promote healthy development and enhance resilience.

Depression is a common and impairing form of psychopathology that typically emerges during adolescence and is associated with suicide and poor academic, vocational, and social functioning (1). Many risk factors for the development of depression have been identified, but critically, not all adolescents with these risk factors develop depression, raising questions about the factors that place adolescents on pathways to resilience. Indeed, resilience is not

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simply the converse of risk and is defined by competence and thriving despite adversity (2). Moving beyond a risk framework to a resilience framework requires consideration of advantageous characteristics and experiences rather than simply detrimental attributes and challenges. Indeed, risk and resilience have a complex association and can both complement and operate at odds with each other, as challenging experiences could enhance the likelihood of problems but also trigger responses that promote adaptive functioning. Because the developmental clinical neuroscience of depression has numerous gaps in understanding resilience, however, pathways related to risk remain the starting point.

This conceptual review extends beyond traditional investigations of group-level differences to examine the interplay of neural social-affective systems and social threat experiences to determine longitudinal pathways of resilience to adolescent depression. We propose a conceptual model and apply it to sexual and gender minority (SGM) adolescents, a population with known disparities in depression and likelihood of social adversity, but also unique resilience factors.

CONCEPTUAL FRAMEWORK

Theoretical Context

Broadly, developmental psychopathology guides this model. From this perspective, depression or resilience is a process with inherent variability and flexibility that occurs against the backdrop of typical social and neural development. Equifinality and multifinality are important concepts describing the possibilities of one outcome occurring through many possible paths and one factor leading to many possible outcomes (Figure 1). Risk and resilience factors can interweave along these paths and produce a variety of outcomes, with flexibility along the way and both positive and pathological outcomes possible. The proposed model has two organizing themes: clinical neuroscience and brain-experience interaction. Individual differences in neural social-affective systems are mechanisms of depression or resilience, and they develop in a social context, both influenced by social threat experiences and modulating the influence of such experiences on the development of depression.

Several conceptual models inspire this model. Affective neuroscience models characterize depression as occurring through alterations in neural reward and threat systems, with resulting difficulty in reducing negative affect and/or enhancing positive affect [e.g., (3,4)]. Cognitive and social models present depression as involving negative beliefs about one’s value or competence, a disrupted notion of one’s place in the social world, or heightened response in threat and self-related circuitry following targeted social rejection (5-8). Developmental models postulate that neural, social, and behavioral changes during adolescence kindle depression when the reward value of social experiences increases and one’s progress toward highly valued social goals is thwarted, with special vulnerability for adolescents who have neural sensitivity to experiences such as social evaluative threat (3,9-11). Neurophilosophy models posit that the fundamental feature of depression is disruption of the self, including the self’s place in a social environment, as embodied by the brain’s resting-state function (12). Developmental psychopathology models further point to the importance of examining the interplay among social and neural factors over time and

in the context of developmental processes (13). Applying a resilience perspective to these models allows us to extend them, integrating central elements and conceptualizing a range of possible advantageous outcomes, including avoidance of depression. While not fitting the traditional model of resilient outcomes, clinical outcomes such as favorable response to treatment, lower severity, and rapid remission after onset fit the current model as they can reflect amelioration of negative outcomes.

Developmentally, adolescence is an optimal period for investigating convergence of social and neural characteristics that lead to depression (13). It is a time of intense neurobehavioral change in affective, social, and identity domains, with balance among systems creating vulnerability (9,14). Notable characteristics of adolescence include sensitivity to reward [e.g., (15)], affective intensity and lability (11,14), and increased valuation of peer social goals such as status, friendship intimacy, and romantic/sexual relationships (16). Self and identity, including sexual orientation and gender identity, also undergo meaningful development during adolescence (17-21). The plasticity accompanying these myriad changes (and their potential interplay) could have developmental implications (22,23), making this period one of opportunity to shift adolescents' development from pathways of risk to those of resilience. Indeed, models of resilience emphasize adolescence as a period in which the foundations of lifelong resilience develop (24).

OUR MODEL: NEURAL AND SOCIAL FACTORS IN RESILIENCE TO ADOLESCENT DEPRESSION

Extending beyond risk-focused models, we emphasize resilience and propose that a key set of pathways involves the combination of social threat experiences and function in neural social-affective systems (Figure 2). As in previous work (13), we define resilience as a dynamic process—rather than a stable characteristic or static event—through which positive adaptation is achieved despite adversity. Resilience can include absence of depression and positive social or academic functioning. Given developmental changes and the recurrent nature of depression, resilience itself can be present at one point and absent at another, or evident in clinical course. Resilience and risk can be seen as opposing processes that unfold throughout development to place adolescents on pathways to depression or health. What appears to generate resilience or depression at one point could have the opposite effect at another. For instance, a social experience could lead, through shifts in social-affective systems, to what appears to be an adaptive outcome in childhood but depression in adolescence.

We postulate that neural social-affective systems modulate the influence of social factors and are also dynamically influenced by those factors. For instance, given the finding of low ventral striatum (VS) response to reward anticipation in adolescent depression (25,26), a stable high VS response to reward could moderate the influence of low childhood socioeconomic status (SES) by buffering adolescents from its influence. In tandem, low SES could influence brain development by blunting VS response to reward, facilitating a pathway to depression. Social experiences themselves can also interact, for example,

through cumulative effects, amplification of some risks' effects by other risks, and distal experiences priming reactivity to proximal experiences.

A novel feature of this model is the identification of temporally distal and proximal factors in adolescent resilience based on developmental vulnerability. Consistent with the notion of periods in which brain development is sensitive to specific experiences (27), some social factors could have influence across development yet have particularly strong influence on adolescent resilience at key points. Based on findings such as the pernicious lasting effects of early adversity on brain development [e.g., (28)], the emergence of associations between depression and reward circuitry at adolescence (29), and the hypothesis that adolescence is a sensitive period for peer social input (30), we identify factors as distal or proximal not by their presence but by their likely periods of greatest impact. Accordingly, parenting during childhood is considered a key distal influence, and peer victimization, bias/discrimination, and identity factors during adolescence are considered key proximal influences. A related hypothesis is that while social-affective systems have important influence on resilience across childhood and adolescence, threat systems might have more childhood distal influence, whereas reward systems might have more adolescent proximal influence on adolescent outcomes. Naturally, developmental change has ongoing impact, with the potential to steer adolescents toward resilience or to create sensitivity to social or neural factors at many points.

CLINICAL NEUROSCIENCE OF SOCIAL-AFFECTIVE SYSTEMS IN DEPRESSION

The clinical neuroscience of adolescent depression (Figure 3) has revealed disruptions in affective neural systems, particularly reward and threat systems [e.g., (3,31,32)]. Because depression is a disorder of impaired social functioning (33) and substantial social development occurs during adolescence, social and self-focused neural systems and social experiences are also likely to contribute.

Reward System

Consistent with the notion that depression involves reduced positive affect and motivation, function in neural reward systems is disrupted in adolescents and adults with current depression. Lower response to reward in the striatum, particularly during anticipation, is consistently reported (26). Notably, low striatal response in depression is of greater magnitude in adolescents than in adults (26), suggesting an important role for development. Depression is also consistently associated with greater response in the orbitofrontal cortex (34,35), medial prefrontal cortex (mPFC) (25), and rostral anterior cingulate cortex (ACC). At a network level, depression is associated with lower functional ACC–orbitofrontal cortex connectivity (36), inflexibility in local ACC-mPFC connectivity (37), and altered within-system connectivity (38). The mPFC has been proposed as a node of altered affect regulation, as it appears to have unstable and more variable functional connectivity in depression both locally (39) and with other networks (40). Reward system alterations are postulated to underlie the cardinal depression symptom of anhedonia, that is, difficulty with motivation for or enjoyment of pleasant events (41).

Reward system function has predictive value: Adolescents with low striatal response to reward exhibit worsening depression symptoms over 2 years (42), and those with low striatal response and greater resting left VS node strength (an index of connectivity) in relation to 10 other reward nodes tend to develop depressive disorders over 3 years (26,43). This system also appears altered in typically developing adolescents at familial risk for depression (44). Its function could thus be a trait marker, present regardless of current mood state or the eventual experience of depression. The literature on stability of function in reward or other systems is sparse, however, and there is a strong need for further investigation. Conversely, a pattern of more typical function in this system—especially greater VS response, based on replication and meta-analytic findings of reduced response in depression (26)—could influence resilience. This could serve a stable protective role or confer imperviousness to the influence of social risk factors. Basic research has revealed that brain maturation involves settling into a pattern of lower variability that effectively reduces the influence of environmental factors (45,46), and resilience could be more likely in humans who emerge from adolescence with a responsive, sensitive reward system.

Threat System

In line with models that emphasize depression as a disorder of intense and poorly regulated negative affect, the neural threat system is excessively reactive in depression. Greater amygdala reactivity to emotional faces (34) and greater response to negative affective stimuli in the dorsal ACC and anterior insula are well documented in depression (47). The subgenual ACC (sgACC) has a long-reported association with depression and clinical relevance, as it was the primary target of deep brain stimulation for treatment-resistant depression (48), and its connectivity is critical for response to transcranial magnetic stimulation (49,50). In adolescent depression, alterations in this system include lower functional connectivity between the amygdala and the ventromedial and dorsolateral PFC (51,52), and greater connectivity between the sgACC and other threat regions (53). Strong within-system connectivity could confer risk for depression, as greater amygdala-rostral ACC connectivity in adolescence predicts depression in early adulthood (54).

Social and Self-processing System

Depression includes alterations of overlapping social and self-processing neural systems, with mPFC and precuneus/posterior cingulate cortex common to both. The temporoparietal junction, a social node postulated to represent self-other distinctions and attributions of others' mental states (55), could be a mechanism of social-affective disruptions in depression, as it is associated with adolescents' positive affect and emotional closeness to others (56). Functional alterations in depression are also widely documented in the default mode network, the set of regions most active during resting state and thought to support self-processing (57,58). Adolescents with depression exhibit greater connectivity within this system during emotional processing and stronger connectivity between the posterior cingulate cortex and the sgACC/VS at rest (59). Posterior cingulate cortex connectivity is greater in adolescents with higher depression severity and earlier age of onset (59), indicating strength of association or possible scarring effects on neural development. Notably, the social system serves as a figurative hub for self, reward, and threat processing disruptions in depression. Social experiences and stimuli elicit greater responses in threat

systems (60), and social anhedonia, a symptom preceding depression and associated with poor treatment response, is linked to altered functioning social and reward systems for adolescents and adults (61,62). When experiencing social threats such as exclusion or rejection by peers, adolescents with depression exhibit stronger responses in threat regions such as the amygdala and anterior insula/ventrolateral PFC (63-65) but weaker responses in social regions such as the lateral temporal lobe (63,66).

Reward, Threat, and Social Systems in Adolescent Depression: Integration

Depression is a network disorder, characterized by both within-network and between-network disruptions. In addition to the above findings, adolescents with depression exhibit higher connectivity between threat and self-processing systems (67) and aberrant ACC connectivity across networks (37). Similarly, adults with depression exhibit weaker connectivity within the reward system (68), greater connectivity between reward and self-processing systems (36), and more variable mPFC connectivity with threat, control, and self-processing systems (40,69,70). Strikingly, adolescence allows a valuable window for understanding alterations in neural systems in depression. The disruptions in reward, threat, and social systems in adolescent depression generally mirror those in adult depression, although in several examples effects are stronger or reflect earlier age of onset.

Still, as suggested by findings that adolescents' recovery from depression (51) and resilience to depression (71) involve different neural pathways than current depression, it would be reductionist to assume that the same patterns of function related to current or future depression are identical to those supporting resilience to depression. Despite extensive research on mean-level group differences and even potential scar effects of depression on brain function [e.g., (37)], there has been little attention to within-person stability or between-person differences. Within-person stability could indicate a trait-like tendency, and between-person differences could inform the understanding of subgroups and multiple pathways in the course of depression.

How Might Neural Social-Affective Systems Contribute to Resilience?

We propose that a stable pattern of function that resembles that of low-risk, typically developing adolescents could promote affect regulation, buffer from the effects of pernicious social experiences, guide toward appropriate responses to social rewards, and encourage development of a robust self. Just as the adolescents who respond to treatment for depression appear to be those with hearty reward system function (29), typical patterns of function could encourage resilience. Adolescents who are resilient to depression despite risk factors exhibit stronger amygdala–orbitofrontal cortex connectivity, which is in turn associated with greater positive life events (71). Evincing responses such as higher VS and lower mPFC activity when anticipating reward, lower amygdala activity when encountering threat, weaker within-network connectivity when processing self-related material, and weaker amygdala–ventromedial PFC functional connectivity when experiencing social threat could buffer against the harm of painful social experiences. At a systems level, an optimal pathway might include balance within and between neural systems. We have yet to learn how these differences play out at an individual level.

Intriguingly, altered function in these systems could be common across psychopathology rather than specific to depression, as noted in recent meta-analyses (72,73). Even within depression, subtypes can exhibit different and sometimes opposite patterns in social-affective systems (4,74)

BRAIN-EXPERIENCE INTERACTION: SOCIAL FACTORS AND THEIR INTERPLAY WITH NEURAL SYSTEMS

What puts adolescents on a pathway to depression or resilience? The contributions of social threat experiences—in addition to or in combination with function in neural social-affective systems—could be informative. Within an ecological model of mental health (75), which recognizes multiple domains and levels of influence, we describe distal and proximal social factors organized into three levels of context: individual, interpersonal, and societal or systemic.

Distal Social Factors

Individual Factors.—Gender and family history of depression are strong contributors to resilience, as girls and adolescents with parental history of depression are at elevated risk for depression (76,77). Maternal history of depression, which also has interpersonal relevance, has been linked to adolescent depressive symptoms via alterations in reward and threat neural systems (78,79). As possible evidence for shared intergenerational reward response, mothers with depression and their adolescent daughters exhibit similar VS response to loss (80). In young children, severity of prenatal maternal depression is associated with altered threat system function: lower connectivity between the left amygdala and the right insula, bilateral VS, and sgACC (81), and greater amygdala response to negative emotional faces (82). These early changes may influence development in threat systems (83), contributing to risk for adolescent depression. Temperament, especially high negative affectivity and low positive affectivity, contributes to adolescent depression, is thought to interact with family processes to influence adolescent depression, and is associated with altered response in the threat system (84-87). Unlike temperament, the role of other stable identity factors in the function of neural social-affective systems unfortunately remains largely unexplored.

Interpersonal Factors.—Parenting has consistent associations with depression, with maternal warmth reported widely as a protective factor (88) and parental conflict, overinvolvement, lower autonomy granting, and aversiveness as risk factors (89). Behavioral observation suggests that parents influence adolescents' depression through encouraging depressive-like behavior and failing to reinforce positive affect (90). High maternal warmth influences adolescent boys' neural response to reward in families with maternal depression (91), and low maternal warmth is related to adolescent girls' depressive severity through greater mPFC response (92). Higher maternal warmth appears to buffer adolescents' threat responding, with lower response to parental criticism in the amygdala, insula, and ACC, and sgACC mediating the association between maternal warmth and depression (93).

Maltreatment—neglect, physical abuse, or sexual abuse—has striking influence on depression (94) and is the focus of a burgeoning literature on brain development (95).

Reward and affective systems are postulated to be especially sensitive to its developmental effects (96), and the age at which maltreatment is experienced could determine its influence on neural circuitry (97). Neglect impairs amygdala and striatal response to social threat and reward, respectively (98,99), and these adaptations may contribute to adolescent depression (100). Numerous studies have linked maltreatment to threat systems via greater amygdala-mPFC connectivity and to reward systems via low VS response to reward (95). Adolescents with a history of maltreatment exhibit increased VS-mPFC connectivity during reward receipt, with this pattern mediating the association of maltreatment with internalizing symptoms (101). Consistent with our model, neural affective systems appear to moderate maltreatment effects, with resilience (or more favorable course of depression) in adolescents with childhood maltreatment and greater striatal response to social reward. Threat system function seems to mediate the influence of maltreatment, with adolescents' lower dorsal ACC response to threat predicting increasing severity of general psychopathology (102,103).

Systemic Factors.—Experiences of otherness and lower social standing compared with dominant or more powerful social groups throughout life contribute to depression. SES is consistently associated with adolescent depression (104,105), but its heterogeneity prevents a full understanding of the contributions of its various components (e.g., financial disadvantage, malnutrition). SES may impair regulation by the PFC and ACC of reward and threat systems (106,107), leading to difficulties in regulating behavior and affect (106). The sparse literature on societal risk factors and brain development hints at influences on reward systems, such as a finding that SES is associated with altered mPFC response to reward, which in turn is related to depression (108).

Proximal Social Factors

Individual Factors.—Identity factors such as race, ethnicity, ability, body size/shape, and SGM status confer risk for depression. SGM identity is described in a subsequent section. Identity may contribute to resilience through the development of a cohesive, multifaceted, stable self that allows adolescents to function in social and academic/vocational domains, manage adversity, and enhance resilience (109).

Interpersonal Factors.—Peer victimization, including bullying, harassment, threats, physical aggression, and relational aggression, is strongly associated with adolescent depression (110). Adolescents' neural threat system response to peer exclusion is associated with both concurrent (64) and future (111) depression. Furthermore, adolescents' neural responses to peer interactions could contribute to depression, as through the combination of past peer victimization and heightened response to social exclusion in the anterior insula and dorsal and subgenual ACC (112) or greater mPFC response and VS-mPFC connectivity to peer reward (61).

Systemic Factors.—Experience of bias and discrimination, or unfair attitudes and treatment based on perceived group membership (113), can have consequences for adolescent depression (114). While these factors are pervasive and lifelong, they could have proximal influence because adolescents' increasingly sophisticated social cognition (115) may enhance their awareness and experience of inequities.

Social Resilience Factors

Positive social experiences, especially when frequent, intense, or occurring across multiple developmental points, could shift adolescents from a pathway of risk to one of resilience. Peer support through intimate friendships, strong social networks, and affiliation with groups such as teams or clubs can bolster resilience (116). Specifically, for adolescents who experience social withdrawal or rejection sensitivity, support from friends can have a buffering influence on the development of depression (117-119). For adolescents with risk factors, there is the optimistic possibility of generating resilience by ameliorating modifiable negative influences (e.g., harsh parenting) or boosting positive influences (e.g., support from friends). Prevention targeted at social factors could improve outcomes through influence on the brain, by sculpting neural social-affective systems or providing a context for those systems to enhance functioning.

SGM ADOLESCENTS: A POPULATION FOR UNDERSTANDING RESILIENCE TO DEPRESSION

The proposed model has relevance to SGM adolescents, who experience depression at 2–4 times greater rates than cisgender/heterosexual adolescents (120-126), putatively owing to the combination of general and SGM-specific social threat experiences. Given this disparity, it is a public health imperative to apply conceptual models to this high-need population to elucidate targets for interventions that enhance resilience. SGM adolescents are considered as a population, with the rationale that while some outcomes can vary by subgroup (e.g., bisexual adolescents), similarities in health disparities and social risk factors are strong (127,128). Furthermore, in our model, SGM adolescents are conceptualized as a group that experiences unique and often intense social threats, not as a group with fundamentally different biological mechanisms than cisgender/heterosexual adolescents. Importantly, greater attention to SGM health will benefit the understanding of both the distinct disparities within that population and the health of the general population (129).

SGM Risk and Resilience to Depression

The most prominent conceptual model of SGM health, minority stress theory (123), postulates that persistent discrimination, prejudice, and stigma result in a chronically aversive and damaging social context, which in turn exerts physiologic effects that result in worsening health. Minority stress is conceptualized as including processes that are external and internal (123) (often termed distal and proximal). External stressors, which are imposed based on SGM status, include discrimination, microaggressions, misgendering, and peer victimization (see Table 1 for definitions). As in our model, external SGM stressors operate on interpersonal (e.g., harassment at work) and systemic (e.g., not including SGM identity in nondiscrimination laws) levels. Internal SGM stressors are intraindividual factors—such as concealing SGM identity, internalizing stigma, and anticipating rejection—that putatively protect mental and physical well-being in the short term but generate health risks in the long term. Both types of SGM stressors are associated with depression (130-137).

In SGM adolescents, the developmental burden of social threat is high. In addition to SGM-specific stressors, adolescents in this population experience higher rates of childhood

sexual abuse (odds ratio = 3.8) and physical abuse (odds ratio = 1.2) (136,138,139) and greater likelihood of polyvictimization than those who do not identify as SGM (140).

SGM adolescents also experience unique resilience factors. A developmental task—and opportunity—of adolescence is developing a positive and cohesive self, and SGM adolescents who develop a positive identity alongside coping strategies for living with a stigmatized identity have strong mental health outcomes (141). Among SGM individuals who experience victimization (141), actual and perceived parental acceptance of, and advocacy for, SGM identity promotes resilience to depression. Finally, systemic supports during developmental periods of vulnerability (e.g., gay-straight alliances in schools) reduce depression and enhance well-being (142).

We propose that adolescents' resilience in the face of SGM stress involves interaction with function in neural social-affective systems. SGM adolescents with typical and invulnerable patterns of response in reward, threat, or social/self neural systems may more readily withstand identity-related stress to develop along healthy pathways. Neural mechanisms of pathways to depression or resilience in SGM adolescents have been woefully ignored, however, and this has prohibited opportunities for prevention and treatment.

While many studies address the disparities in depression and risk and protective factors in SGM youth, few have addressed the interaction of experiences related to SGM identity with reward, threat, and social/self systems. Research has focused on threat systems in sexual minority young adults (143) and women (144), indicating elevated cortisol in sexual minority women (143) and blunted cortisol (143) and elevated heart rate (145) in sexual minority men. Altered resting cortisol profiles also correspond to SGM-specific stressors, such as using public bathrooms or living in states with unprotective nondiscrimination laws (146,147).

One preliminary study on reward suggests that temporoparietal junction response to social reward could mediate associations between sexual minority status and higher interpersonal depressive symptoms (148). While limited by a focus on neural but not social factors, this study provides a step toward describing altered neural social-affective systems as a risk for this population. Future investigations should include level of SGM stress and cumulative social threat across general and SGM categories and resilient outcomes.

FUTURE DIRECTIONS AND CLINICAL IMPLICATIONS

There is ample room for research on adolescents' pathways to resilience. Studies with longitudinal, prospective designs can investigate development in neural social-affective systems, experience and timing of social threat experiences, and interactions among neural and social factors. Such designs will allow greater depth of knowledge of social factors, for example through within-person analyses that allow research to extend beyond mere parental warmth to consistency of warmth. Notably, because resilience is a complex process, it will be critical to investigate how factors might confer resilience at some developmental points (or during a time window following an event) but risk at others. A notable example of this possibility is the seemingly precocious strengthening of amygdala–ventromedial

PFC functional connectivity in children who have experienced maltreatment (149), a potentially adaptive change during immediate circumstances that could have consequences for psychopathology and brain health in the longer term.

We call for the field to increase understanding of the development of resilient adolescents, including SGM adolescents, especially those who shift from higher-risk to higher-resilience pathways. At even greater detail, computationally intensive approaches will allow detailed investigation of individual pathways toward resilience (150).

Resilience in SGM adolescents can be promoted through two psychosocial approaches: 1) intervention with families, peer groups, and schools to promote acceptance and support; and 2) direct work with SGM adolescents to reduce internalized stigma, bolster skills for managing responses to social threat, and embrace SGM identity. At a clinical level, mental health providers should be trained to incorporate SGM-affirmative approaches. At a societal level, efforts should promote SGM rights, ensure SGM access to mental health resources, and guide communities, schools, and states toward policies to support SGM adolescents. These interventions can have measurable effects on the neural systems and brain-experience interactions that underlie pathways to resilience.

CONCLUSIONS

Resilience to adolescent depression occurs through many possible pathways, with neural social-affective systems and proximal and distal social experiences playing crucial and interdependent roles. Development contributes to resilience, providing opportunities to identify, understand, and promote routes to healthy outcomes. For high-need SGM adolescents, additional identity-related social threat experiences make resilience a more challenging goal but could underscore the critical influence of neural social-affective systems. Research and clinical priorities should consider the importance of neural social-affective systems and target modifiable social threat factors.

ACKNOWLEDGMENTS AND DISCLOSURES

The authors' research is supported by the National Institutes of Health (Grant No. R01 MH104418 [to EEF], Administrative Supplement 06A1S1 to R37 MH100041 [to KLE; principal investigator, M.L. Phillips], and R01 MH103241 [to JSS]) and funding from the Health Resources and Services Administration, U.S. Department of Health and Human Services (to DLR).

We thank Morgan Lindenmuth and Melissa Nance for assistance with formatting and references.

EEF has received an honorarium from the Association for Psychological Science and consulting fees from Case Western Reserve University, Brown University, and Otsuka/Durham VA. The other authors report no biomedical financial interests or potential conflicts of interest.

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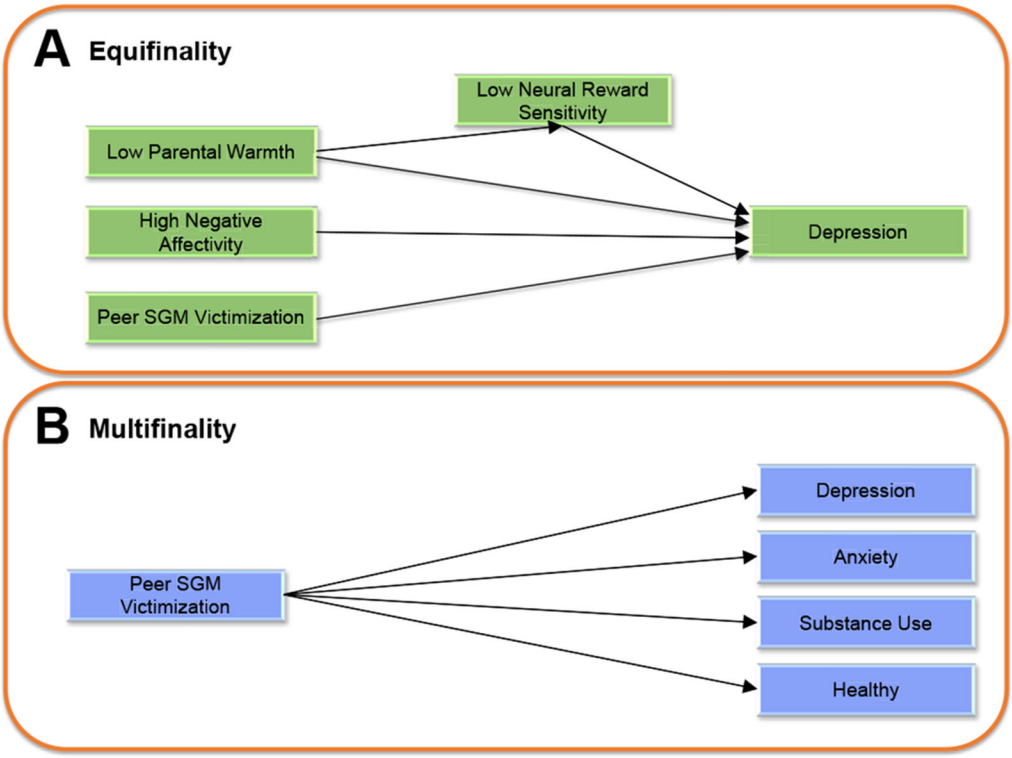

Figure 1.

Variability and flexibility in development of adolescent depression through processes of **(A)** equifinality, in which depression may occur through multiple possible pathways representing combinations of contributing factors, or **(B)** multifinality, in which one factor may lead to many possible outcomes through different pathways. SGM, sexual and gender minority.

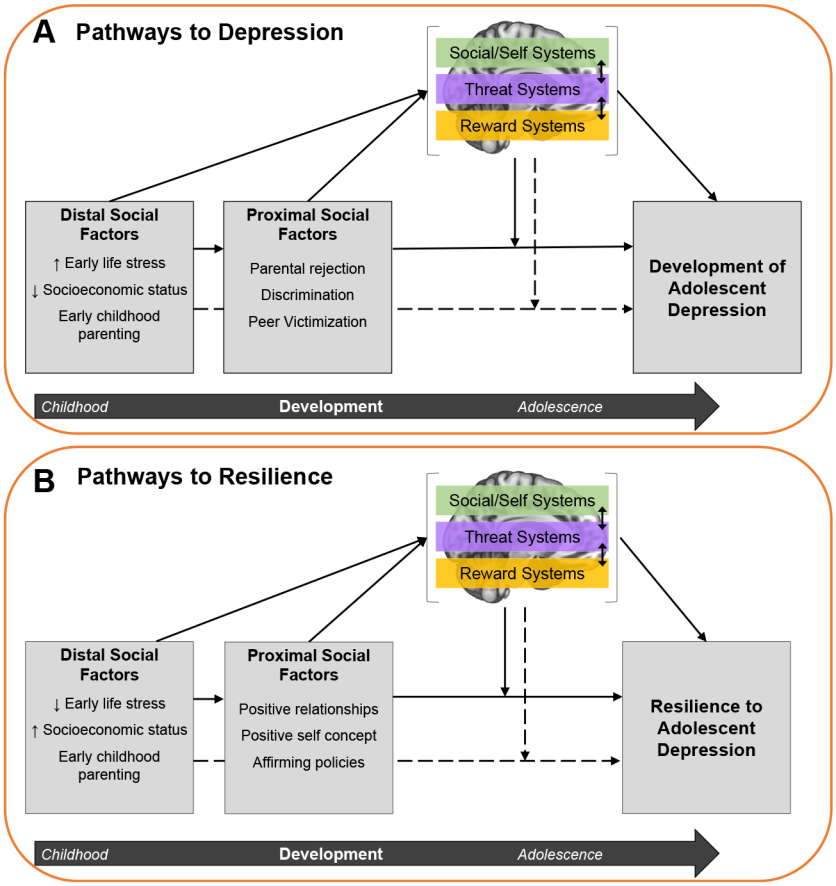

Figure 2.

A social-affective neuroscience model of adolescent depression and resilience, where depression or resilience are shaped through a combination of distal and proximal risk/resilience factors interacting with social-affective neural systems, with multiple opportunities for intervention. Important risk and resilience factors may vary by identity group, and these factors are paramount when considering interventions.

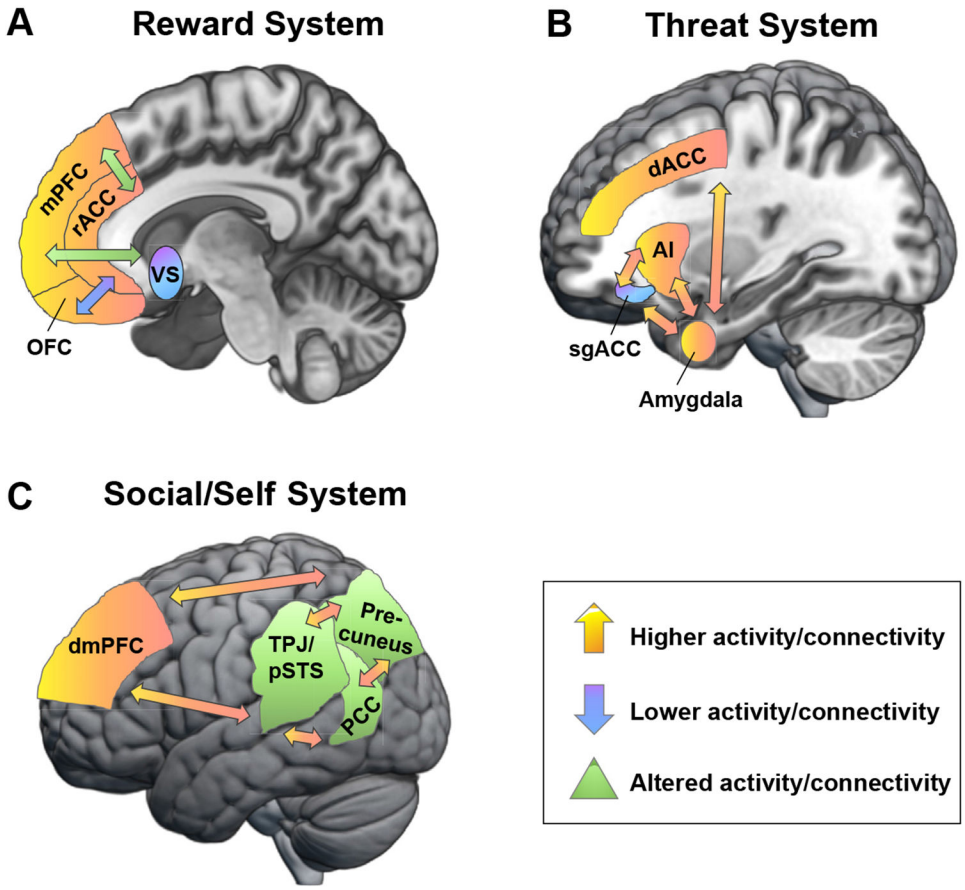

Figure 3.

Critical nodes of adolescent depression within reward, threat, and self/social neural systems. **(A)** Within reward neural systems, adolescent depression is associated with lower VS and increased mPFC, rACC, and OFC activity to reward, as well as altered connectivity among these regions. **(B)** Within threat neural systems, adolescent depression is characterized by high amygdala, dACC, and AI activation to threatening stimuli, lower activation of the sgACC, and increased connectivity among these regions. **(C)** Within social/self neural systems, adolescent depression is characterized by high dmPFC activity to social reward stimuli; altered engagement of the TPJ/pSTS, precuneus, and PCC; and increased connectivity among these regions. AI, anterior insula; dACC, dorsal anterior cinculate cortex; dmPFC, dorsomedial prefrontal cortex; mPFC, medial PFC; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; pSTS, posterior superior temporal sulcus; rACC, rostral ACC; sgACC, subgenual ACC; TPJ, temporoparietal junction; VS, ventral striatum.

Table 1.

Internal and External Stress Factors for SGM Adolescents

Factor	Definition
Internal Stressors	
Internalized Stigma	Negative stigma, prejudice, and stereotypes against SGM groups turned inwardly (e.g., internalized homophobia)
Expectations of Rejection	Expectation of stigma based on a knowledge of society's stance toward SGM groups
Identity Concealment	Intentional nondisclosure of a socially stigmatized identity (e.g., sexual orientation, gender identity)
Social Identity Threat	The fear of being discriminated against because of a marginalized identity
External Stressors	
Microaggressions	Subtle intentional or unintentional demonstrations of discrimination, including microinsults (insensitive behaviors and comments), microinvalidations (behaviors and comments meant to invalidate a person's or group's experience), and microassaults (negative comments denigrating a person's identity)
Misgendering	Microaggression against people who are transgender and/or nonbinary, involving intentionally ignoring or invalidating a person's gender and chosen gender identifiers (e.g., use of incorrect gender pronouns, use of a name assigned at birth instead of a chosen name)
Discrimination	Unjust treatment based on being part of a minority group
Peer Victimization	Physical, verbal, or psychological abuse by peers with intent to cause harm

Classification into internal and external (frequently termed proximal and distal) stressors is based on the minority stress theory proposed by Meyer (123), which conceptualizes proximal stressors as internal processes related to the self and distal stressors as external and imposed on the individual.

SGM, sexual and gender minority.