The Effects of Stress and Depression on the Adolescent Brain

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Abstract

Adolescents are particularly vulnerable to deteriorating mental health due to greater brain plasticity and being in a developmental phase. Brain plasticity involves the brain's capacity to adapt to experiences and environmental factors. There is evidence suggesting that the adolescent brain is particularly susceptible to environmental stress and risky behaviors. This paper will investigate a connection between the cognitive changes that accompany deterioration in mental health and those that accompany excessive stress in adolescents. Studying the neural responses in adolescent brains can give us important insight into the effects of stress and mental health on individuals and how the neural responses themselves contribute to driving this behavior. Here, I will explore the activity in several brain regions related to reward, loss, and cognitive control, all of which can be altered due to acute stress and depression in adolescents. Knowledge about the changes that the adolescent brain goes through during stress and depression and their similarities can help us find possible markers of depression.[1] The goal of this paper is to express the effects of stress and depression on the adolescent brain and propose further research in a direction that can help the adolescents of the world.

Discussion

Effect of Depression and Stress on Reward and Loss Brain Regions

The theory of emotional context insensitivity states that depression is characterized by a flattening of all stimuli, both positive and negative. This emotional insensitivity can increase susceptibility to mental illness, alter brain structure, destroy neurons, shrink brain volume, and impact cognition.[3] It is important to investigate the underlying mechanisms of depression that create this emotional insensitivity, as it can impact an individual's overall quality of life and emotional well-being. The progress being made in the study of adolescents and their neural responses to stress and depression is an important first step to these more longitudinal understandings of the impact on quality of life and emotional well-being. The effects as mentioned earlier, however, have predominantly been researched in adults. Adolescent studies are often harder to conduct as subjects are minors and require more permissions when it comes to being part of a study. As of late, however, a growing body of literature is focused on exploring the effects of stress and depression on reward and loss brain regions in adolescents, where brain processing can differ from adult processing.

The effect that different stimuli have on activity in the reward regions of the brain can be altered by stress. These changes in neurological responses may serve as early indicators of depression as people with depression are shown to have different neural activity from people who do not have depression.[8] To study the effect of depression symptomatology on reward-related behavior and resulting neurological processing, scientists ran an experiment in which patients had to press buttons as fast as possible to either get a desirable (chocolatey) drink faster or try to avoid the undesirable (moldy) drink. It was found that adolescents with depression symptomatology were less inclined to try as hard as adolescents without depression symptomatology in the tasks of avoiding the moldy drink or trying to attain the chocolatey drink.[3] Adolescents shown to have a reduced/ lower response to a stimulus in the parts of the brain related to reward, such as the cingulate cortex, are more likely to be at a higher risk for depression, (Figure 1). The brain region activity involved in an effortful motivation to win reward and risk aversion in adolescents is reduced in adolescents at risk for depression, essentially meaning that they will work less to achieve something positive and also to avoid something negative. This falls in line with the emotion context insensitivity theory in which depression is characterized by a flattening to all stimuli, both positive and negative.[3]

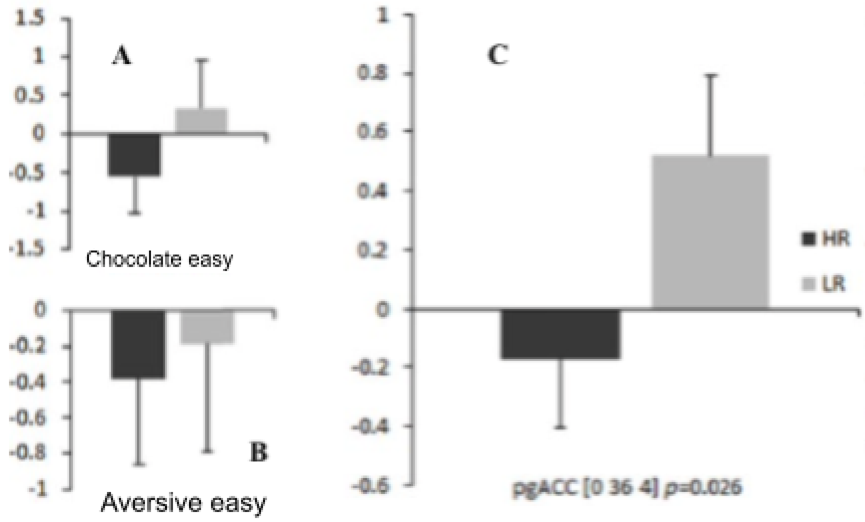

Figure 1: pgACC Activation. Contrast estimates, a proxy for representations of neural activity, in a low-risk (LR) and high-risk (HR) group when experiencing the chocolate easy condition (A). Contrast estimates for LR and HR when experiencing aversive easy conditions (B). Subtraction of chocolate easy and aversive easy conditions for both HR and LR groups shows a much greater difference in brain activity between aversive and appetitive conditions in low-risk groups than in high-risk groups, suggesting that processing to positive and negative stimuli is similar in high-risk individuals (C).[3]

Building on the last experiment's findings of effort expenditure for reward, Lincoln *et al*. studied how stress was affected when working towards monetary rewards. In this experiment, stress was induced using a complex Chatroom Task alongside a Guessing Task involving monetary outcomes. The Chatroom Task involved adolescents interacting with preprogrammed profiles, inducing stress, and subsequently affecting their performance in the subsequent Guessing Task.[10] The striatum is a brain region that links motivation to motor movements involved in the execution of simple motor tasks as well as more complex cognitive tasks, such as reward processing, decision-making, and social interactions.[9] The left dorsal striatum, specifically, is linked to reward-learning learning or operant conditioning. During the stress condition, there was reduced activity in the striatum compared to the no-stress condition. In addition to the blunted neural activity in the striatum, it was found that the stress did not potentiate neural responses to losses, but instead decreased neural responses to wins in loss and rejection-related regions such as the dACC and left anterior insula.[10] Among studies that looked at adolescent stress exposure effects into adulthood, seven showed that the negative effects of stress observed during adolescence on either cell proliferation (a process by which a cell grows and divides to produce two daughter cells), hippocampal neuroplasticity, cognitive deficits, and depressive-like behavior, had a variable impact in adulthood.[14,15] These changes in reward receipt and loss in response to stress may be indicative of a stress-elicited anhedonic-like pattern of neural activation. This means that this experience of stress can cause diminished neural responsivity in reward-related regions, which may be a factor for the diminished positive affect that is often used to characterize adolescent depression.[10] Acute stress contributes to this blunted activation in the left dorsal striatum and also leads to self-ratings of lower positive feelings and higher negative feelings in the participants (Figure 2).

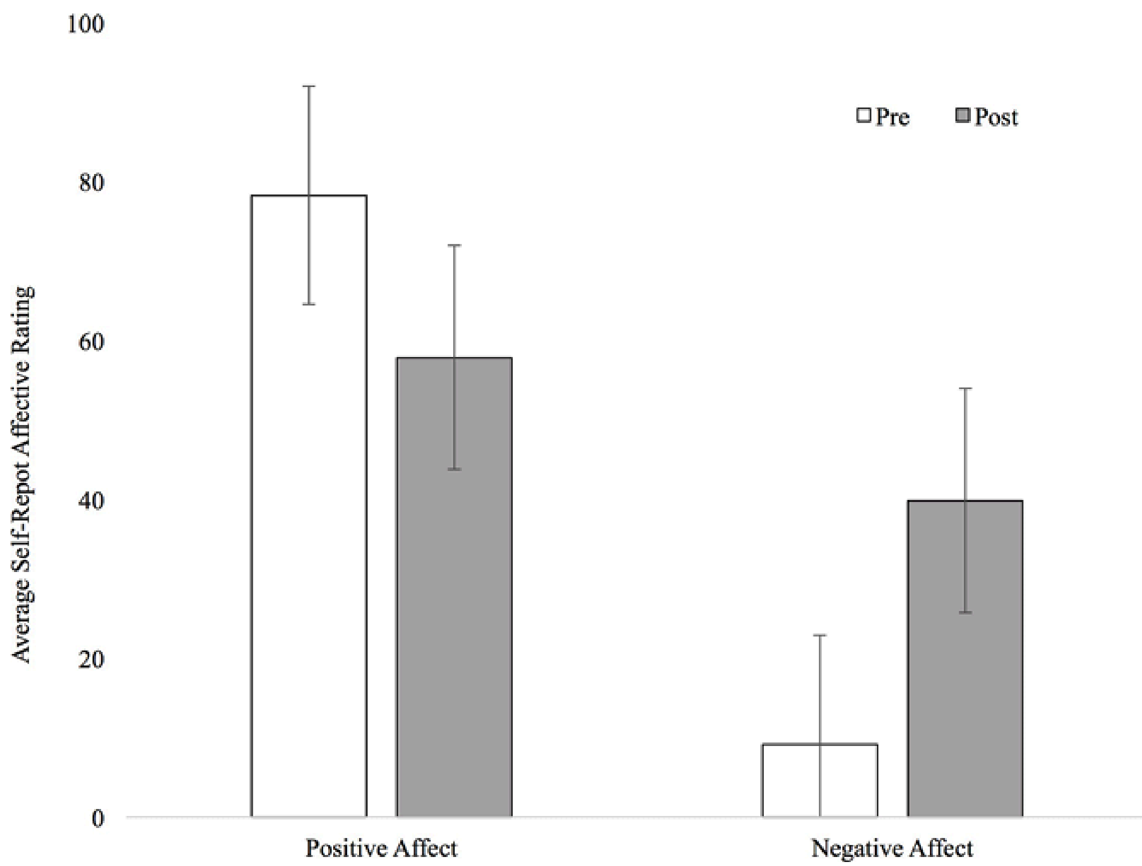

Figure 2: Self-ratings of stress. Self-reported ratings of feelings of both a positive affect and a negative affect both before (pre) and after (post) the stress condition. re-stress there was a low rating for negative affect and a high rating for positive affect, and after the stress conditioning, the positive affect rating went down while that for the negative affect went up.[10]

In a study done by Lewis *et al.*, we can see a Pavlovian stressor task, where college students were shown shapes and then their monetary value while having the stressor (a gel cold pack) on their arm. Cortisol levels were taken from the saliva before the trials, after the first trial, and at the end of all the trials. In the results, it was found that acute stress rendered the ventral striatum more sensitive to the magnitude of positively conditioned stimuli, and this may be related to stress-related increases in cortisol.[11] It was also found that levels of circulating cortisol affect Pavlovian Conditioning. This could mean that stress will affect adolescents' learning ability, specifically reward-based learning. During adolescence, the hypothalamic-pituitary-adrenal (HPA) axis, which is the main stress response system of the body, becomes increasingly reactive to stress, with teenagers exhibiting greater stress-induced cortisol levels than children.[12] Studying the cortisol release in the adolescent age group is pertinent because in adolescents aberrant cortisol secretion following acute stress, marked by either increased release or blunted reactivity, can predict the development of mental illnesses.[11] Acute stressors activate the autonomic nervous system and HPA axis, which results in biological changes such as reduced high-frequency heart rate variability, increased heart rate, cortisol release, and alterations in our neural activity (Figure 3). The stress group was split up into two groups, the cortisol responders and cortisol non-responders. Responders had to show a cortisol concentration change of at least 15.5% and those who did not were placed in the non-responders group.

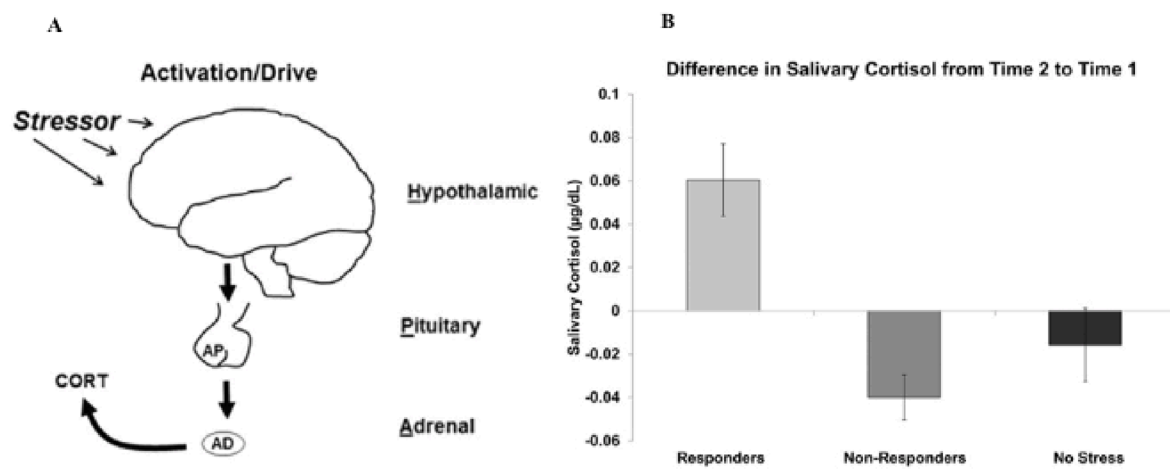

Figure 3: HPA Axis and Cortisol Release. (A) HPA Axis in function, with the stressor affecting the hypothalamic parts of the brain, leading to signals to the pituitary and adrenal glands, ending in the production of cortisol.[12] (B) Effects of stressors on the “Responders” group. They have larger amounts of salivary cortisol after the stressor, while the no-stress and non-responders have much as they have not felt the effects of the stressor.[11]

Activation of front-limbic regions involved in stress regulation is modulated by cortisol, and neural and endocrine systems undergo major development during adolescence. Limbic regions include the hippocampus, ventral striatum, and putamen, which play a part in learning and memory, motivational processes and behavioral outputs, and motor control respectively. This means that it is necessary to study the relationship between neural and hormonal responses to stress to elucidate how neurobiology may drive the onset/early onset of anxiety disorders. Scientists used a computerized MIST (Montreal Imaging Stress Task), a series of mechanical mental arithmetic challenges, while a stressful rising tone while being told that their scores were merely average, no matter how well they were doing. Subjects self-reported higher stress levels, the average MIST heart rate was more significant than the resting heart rate before and after the MIST, and post-MIST peak cortisol was greater than pre-MIST across all subjects. It was found that hippocampal deactivation, negatively affecting learning and memory, was correlated with cortisol release and that trait anxiety is associated with greater ventral striatum activity and reduced putamen activation.[13]

The impact of stress and depression on reward and loss regions of the brain reveals significant alterations in neural activity. Individuals experiencing depression exhibit distinct neural responses in the reward regions, acting as potential early indicators of depressive tendencies. Younger individuals with diminished responses in reward-related brain areas are at a higher risk of developing depression. Moreover, adolescents at risk for depression demonstrate reduced motivation for both pursuing rewards and avoiding negative outcomes, aligning with the emotion context insensitivity theory associated with depression. Stress further emphasizes these effects, leading to blunted neural activity in the striatum during stress conditions, particularly affecting responses to wins in loss-related regions. This stress-induced pattern of diminished responsivity in reward-related regions may contribute to the reduced positive affect characteristic of adolescent depression.[3] Acute stress, as indicated by cortisol release, influences the left dorsal striatum linked to reward-related learning, potentially impacting adolescents' learning abilities. Stress-induced changes in the autonomic nervous system and hypothalamic-pituitary-adrenal axis during adolescence underscore the relevance of studying neural and hormonal responses to stress in understanding the onset of anxiety disorders.[13] Notably, stress and depression affect both reward and loss regions, shaping the neural landscape in ways that may contribute to the development of mental health issues in adolescents.[1-6]

The research discussed throughout this paper sheds light on the significant impact of stress and depression on the activity between the brain's reward and loss regions. The theory of emotional context insensitivity holds in the context of adolescents, especially when it comes to the social stressors that may help shape their personality later on. Adolescents with depression symptomatology exhibit lower motivation and effort in tasks related to both seeking rewards and avoiding losses, mirroring the emotional insensitivity theory perfectly. Moreover, stress negatively amplifies these effects, resulting in reduced responses to both wins and losses in the brain regions that are associated with the sensations of winning and losing. Stress-induced change in reward and loss processing can contribute to the diminished positive effect that can often be observed in those with adolescent depression. Importantly, the research shows an intricate relationship with stress, depression, hormonal responses, and neural activity during adolescence, which can play a critical role in the development of mental health disorders and further complications.

Impact on Emotion

Through adolescence, the brain is continuously growing, and traits such as emotional learning and other actions that link emotion to action continue to develop throughout this period. The amygdala is in a state of growth as well, which is very important because the amygdala is responsible for the perception of emotions such as anger, fear, and sadness, as well as the controlling of aggression.[16] This information was supported by a study done in Oxford by Park *et* *al*. Information such as recent deaths in the family, divorces, chronic illness, and more were all taken and ranked so that scientists had a rough idea of how much stress the adolescent had experienced recently.[17] After scans were taken it was shown that greater exposure to stressful life events was significantly correlated with weaker functional connectivity between the bilateral amygdala and bilateral mPFC, meaning that the adolescents would be more susceptible to aggressive behavior and attention problems in addition to overarching mental health problems (Figure 4).

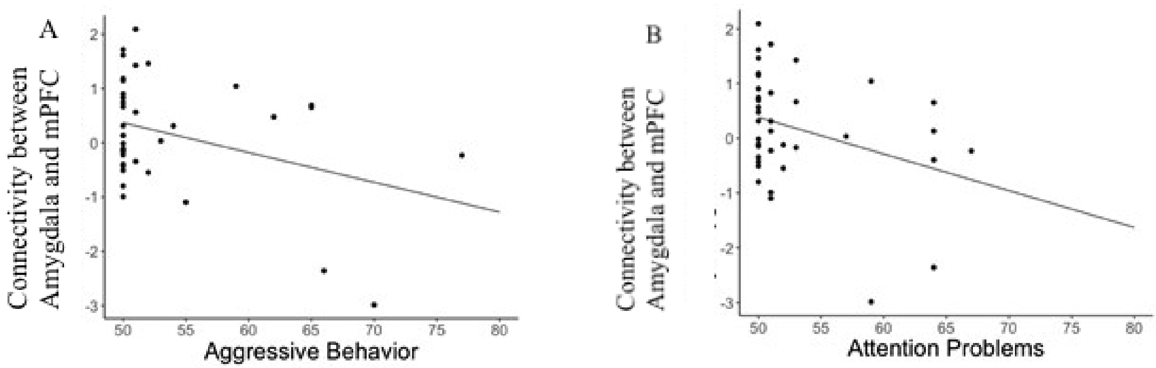

Figure 4. **Effects of Weaker Functional Connectivity**. In part A it is shown that lower connectivity is correlated with aggressive behavior in subjects. Part B shows that attention problems can also arise in adolescents who have lower connectivity between the Amygdala and mPFC. This lower connectivity is caused by stressors in the adolescent developmental period.[17]

Tottenham *et al*. also explored the impact of stress exposure on the developmental changes in affective neurobiology during adolescence, specifically focusing on the amygdala, prefrontal cortex, and ventral striatal dopaminergic systems. Adolescence leads to significant changes in the brain and this period of protracted development can provide both opportunities for learning as well as vulnerability to the effects of stress. To conduct their research, Tottenham *et al*. reviewed existing human studies and integrated insights from animal models that could provide more precise control over the timing of stress exposures. In their study, stress was defined as any environmental challenge that threatened well-being, and could come in various forms, including chronic stress, early-life stress, and acute stressors. These changes can lead to behavioral changes regarding increased fear reactivity. Adolescents who have reported significant traumatic stress in the past year also are more likely to exhibit an amygdala trajectory similar to adolescents with a significant familial risk for depression. This suggested that the amygdala hyperactivity experienced by adolescents who went through significant stressors might be an important biomarker for mental illnesses and identifying the mechanisms targeted by exposure to stress and how they can change the brain during adolescence is central to understanding the development and emergence of mental illnesses.[18]

Conclusion

We have navigated the intricate labyrinth of stress and depression's profound influence on the developing adolescent brain. Adolescence, marked by heightened brain plasticity and a phase of remarkable development, serves as a pivotal juncture for comprehending how environmental stressors can sculpt someone's mental and emotional well-being. The thesis of the paper revolves around establishing a connection between the cognitive transformations linked to declining mental health and those that come from the relentless pressures experienced by adolescents.
Throughout the paper, we have scrutinized the effects of stress and depression on specific cerebral regions associated with reward and loss. Stress and depression can lead to dulled neural responses within these regions, hampering one's capacity to savor the joys of life, respond to positive stimuli, and contend with everyday adversity with all their might. This emotional numbness, as made clear by the emotion context insensitivity theory, exerts major effects on motivation, enthusiasm for pleasurable activities, and overall emotional well-being. This is significant because this means that adults should be trying to protect adolescents from high-stress environments to combat a higher chance of those adolescents having mental health issues. The fact that adolescents are particularly vulnerable due to the growing nature of their brains places more responsibility on us as researchers to make sure that nothing untoward happens to them in this crucial stage of their life that could have unimaginable implications for the children in the future.

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