

# Effect of Anxiety on the Children Brain Structure: Consequences for Children Emotional Healthiness

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**Abstract** - Significant changes in emotional and cognitive functioning, as well as an increase in stress-related psychiatric disorders like anxiety and depression, are all related to adolescent growth. Additionally, the brain is undergoing tremendous maturation at this period, as evidenced by structural changes in numerous limbic and cortical regions. Although the adolescent-related alterations in these regions have been well-described by numerous exquisite human neuroimaging studies, surprisingly less is known about these changes in non-human animals.

Furthermore, there is a dearth of information on how prolonged stress exposure may impair this structural maturation in both human and non-human species. Given the essential link between the structure and function of the nervous system, it is crucial to comprehend how these normal and stress-related structural changes during adolescence affect psychological function, which in turn might affect subsequent neural development.

This succinct overview aims to describe the effects of chronic stress exposure on brain regions that continue to develop structurally during adolescence and are extremely sensitive to its effects. This review will pay special attention to the morphology of the amygdala, hippocampal formation, and prefrontal cortex. Future research directions are also explored because there are still many unresolved issues in this field of study. To better comprehend the mechanisms underlying the rise in stress-related psychiatric dysfunctions frequently seen during this period of development, we must have a clearer understanding of how stress impacts teenage brain development.

**Keywords:** Amygdala, Hippocampus, Prefrontal Cortex, Puberty, Stress, Adolescence.

## I. INTRODUCTION

The structural maturation of the teenage brain has drawn more attention since the seminal reports on longitudinal

magnetic resonance imaging (MRI) investigations were published in the late 1990s (Giedd et al., 1999; Paus et al., 1999; Sowell et al., 1999). The major changes in cognitive capacities and emotional regulation seen during adolescence have been attributed to the morphological changes brought on by puberty in the cortical and limbic brain regions (Miller and Jacobs, 1984). (Giedd et al., 2015).

Researchers have started looking into elements that might interfere with the teenage brain's normal development as well as the short- and long-term effects of these disturbances in tandem with the increased interest in this development (Giedd and Rapoport, 2010). Due to the enhanced experimental control and cellular clarity of animal studies, these disruptions of teenage brain maturation have been viewed from a more mechanistic perspective. This succinct review aims to highlight studies that looked at the neuroanatomical effects of stress on the developing teenage brain. This review will pay particular attention to the effects of stress on the morphology of neurons and indicators of structural plasticity in three brain areas: the amygdala, hippocampus, and prefrontal cortex. These areas are particularly sensitive to stress and have distinctive developmental patterns during adolescence.

Increasing evidence suggests that adolescent exposure to prolonged stress has detrimental impacts on a variety of neurobehavioral outcomes, notably in terms of emotionality (Eiland and Romeo, 2013; Hollis et al., 2013; McCormick, 2010; McCormick and Mathews, 2010; McCormick et al., 2010; McCormick and Green, 2013). It should be mentioned that while this stage would probably last between 10 and 18 years in humans, adolescent development in rodents like mice and rats spans ages that range from 30 to 60 days (Eiland and Romeo, 2013).

Adolescence may bring about a unique susceptibility of the brain to stress and stress-related adrenal chemicals, like the glucocorticoids, as a result of the confluence of a number of elements (i.e., cortisol in primates and

corticosterone in many rodent species; Romeo, 2013). Prepubertal animals (25–30 days of age) show prolonged stress-induced corticosterone responses compared to adults, especially in response to stressors with both physical and psychological attributes (> 65 days of age; Romeo, 2010a; Romeo, 2010b; Romeo et al., 2013). This has been shown in studies on rats and mice.

The mid-adolescent (42 days of age) and adult (67 days of age) rats treated with equal amounts of corticosterone display distinct gene expression profiles, suggesting that the teenage brain may be more responsive to corticosterone. This study, in particular, demonstrated that corticosterone-induced glutamate receptor subunit expression was higher in the mid-adolescent hippocampus compared to adult hippocampus.

## II. THE ADOLESCENT AMYGDALA AND STRESS

The basolateral, central, and medial nuclei are among the sub nuclei that make up the amygdala, which also plays a significant role in mediating fear learning, reward, aggression, and sexual behavior (LeDoux, 2007). According to human MRI studies, both boys and girls' overall amygdala volumes rise from childhood to the beginning of adolescence, peaking at between 12 and 14 years of age for boys and girls, respectively (Goddings et al., 2014; Hu et al., 2013).

It is important to note that after these peaks in expansion, boys continue to show minor increases in amygdalar volume until young adulthood, while girls exhibit slight volumetric decreases. Although these trajectories are further shaped by the pubertal status of the individual and show hemispheric differences, it is important to note that these peaks in expansion occur in the male and female (Goddings et al., 2014; Hu et al., 2013). Animal studies in rodents, including rats and hamsters, demonstrate pubertal-related volumetric increases in sub nuclei of the amygdala, such as the basolateral and medial nuclei, in addition to these human findings (Cooke, 2010; Romeo and Sisk, 2001; Rubi now and Juraska, 2009). Changes in the amount of circulating gonadotropins may control these changes in part (Cooke, 2010; Romeo and Sisk, 2001). Early adolescence in male and female rats is characterized by increases in dendritic length and complexity of neurons in the basolateral nucleus. This volumetric increase in the basolateral nucleus appears to be mediated by expansion of the neutrophil.

## III. THE ADOLESCENT HIPPOCAMPAL FORMATION AND STRESS

The hippocampus and dentate gyrus make up the hippocampal formation, an important part of the brain that mediates a variety of learning and memory processes as well as emotional functions and stress response (Fanselow and Dong, 2010). Neuroimaging studies demonstrate that males and girls' hippocampal volumes expand linearly early in adolescence, similar to the amygdala, and then begin to lose volume in females while continuing to grow in males throughout late adolescence (Goddings et al., 2014).

Studies on non-human animals also document structural changes in the hippocampus formation that are associated to adolescence, with female rats exhibiting increased

dendritic branching between days 44 and 51, followed by decreased dendritic branching between days 51 and 55. (Chowdhury et al., 2014). Additionally, although the density of dendritic spines remains relatively constant throughout these years, the frequency of spines with a more stable, mature appearance (such as those with a mushroom shape) rises during these ages (Chowdhury et al., 2014). On the other hand, research on prepubescent male mice reveals increased spine densities on the dendrites of hippocampal pyramidal and granular cells. However, these changes are curvilinear, so that spine densities increase during the early stages of puberty and then decrease during the transition into young adulthood (Meyer et al., 1978).

Research on the effects of stress and chemicals linked to stress on the size of the hippocampus formation and the morphology of its neurons has been quite extensive in adults (McEwen et al., 2016). Hippocampal volume specifically linked negatively with reported stress levels in postmenopausal women (Gianaros et al., 2007). It is important to note that patients with Cushing's syndrome, a condition characterized by hypercortisolemia, similarly show lower hippocampus sizes (Starkman et al., 1999a). The cellular basis of these structural changes is yet unknown due to the spatial resolution limitations of neuroimaging, however non-human animal research would suggest that these volumetric modifications might be mediated by reductions in dendritic branching of hippocampal neurons.

For instance, research on adult rats has revealed considerable dendritic atrophy in cells of the hippocampus and dentate gyrus after prolonged exposure to relatively high amounts of glucocorticoids or chronic restraint stress (McEwen et al., 2016). These effects of stress on neuronal morphology are reversible, and within ten days after the stressor's cessation, neuronal branching patterns can recover to their pre-stress levels (Conrad et al., 1999). Accordingly, after successfully treating patients with Cushing's syndrome, the abnormally high levels of cortisol are reduced, and hippocampus sizes return to normal (Starkman et al., 1999b). These studies collectively show that the hippocampal formation is vulnerable to long-term stress and stress-related hormone exposure, but that these effects can be reversed with adequate time.

Prefrontal cortex undergoes striking anatomical changes during adolescence. From childhood to the commencement of puberty, the volume of the prefrontal cortex was seen to rise (Giedd et al., 1999; Gogtay et al., 2004; Sowell et al., 1999). The period of cortical thinking associated with adolescence is thought to be partially caused by synaptic pruning and programmed cell death, according to neuroimaging data and histological studies in postmortem human and non-human adolescent brain tissue (Huttenlocher, 1979; Juraska and Markham, 2004; Markham et al., 2007). According to Stores -Baryon et al. (2006), the prefrontal cortex is crucial for controlling emotional behaviors, executive function, and fear extinction. As a result, these structural changes have been proposed to moderate some of the psychological function changes associated with adolescence (Blakemore and Choudhury, 2006; Casey et al., 2010; Ernst and Mueller,

2008; Giedd and Rapoport, 2010; Somerville and Casey, 2010; Yurgelun-Todd, 2007).

The adult medial prefrontal cortex exhibits considerable structural changes after prolonged exposure to either stress or glucocorticoids, just as the amygdala and hippocampal formation (McEwen et al., 2016). In particular, dendritic branching and spine density in pyramidal cells in layer II/III of the prefrontal cortex are reduced (Cook and Wellman, 2004; Liston et al., 2006). (Radley et al., 2006). As attention set-shifting is a cognitive function that is hampered by prefrontal cortex lesions (Birrell and Brown, 2000), this structural remodeling of the prefrontal cortex is linked to impairment of attention set-shifting (Liston et al., 2006), indicating a connection between these morphological changes and modifications in frontal-mediated behaviors. Many concerns remain unresolved, despite the fact that it is now evident how chronic stress exposure affects the development of the teenage brain. To gain a deeper knowledge of the connection between stress and teenage brain morphology, it will be crucial to pursue at least three areas of research as the field develops. The first step will be to conduct tests that directly contrast how persistent stress affects the adolescent and adult brains. Studies that have looked at how stress affects the neuronal structure in the prefrontal cortex, hippocampus, and adolescent amygdala suggest that these effects are similar to those seen in adults. The amount of these structural changes brought on by stress in the teenage and adult brains, however, is still unknown.

#### IV. CONCLUSIONS

According to the research review above, exposure to chronic stress has a considerable impact on the structural elements of the adolescent amygdala, hippocampal formation, and prefrontal cortex. Although many of these morphological changes brought on by stress seem to be similar to those seen in adults, no direct comparisons between the teenage and adult cohorts have been conducted. Therefore, it is not yet known whether exposure to prolonged stress throughout adolescence may be especially harmful to the growing brain. Future lines of research will need to look at both the short- and long-term effects of stress on adolescent brain structure due to the rise in stress-related psychological vulnerabilities during this critical stage of development (Andersen, 2003; Dahl and Gunnar, 2009; Eiland and Romeo, 2013; McCormick and Green, 2013). Establishing the precise impact of stress-induced structural changes in adolescent people's mental health and wellbeing as they enter young adulthood and beyond will also be crucial.

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