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# Association Between Prenatal Stress and Offspring Mental Growth and Behaviour-A Review

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## ABSTRACT

*Gestation is an important period in a reproductive life of a female. It is a time of development of an embryo into a fetus inside the womb of the mother. A mother experiences many changes during this phase both physically as well as mentally. Research that investigated maternal anxiety and depression during pregnancy have shown significant associations with emotional problems in children. Prenatal stress activates HPA axis inducing the release of several hormones, including cortico-releasing hormone (CRH), ACTH, cortisol and adrenaline in the bloodstream. Studies on animals explained that whatever be the type of stressor repetitive restraint stress or any unpredictable stressors, offspring's of both genders showed decreased proliferation cells in the dental dyrus of brain and significant reduction in hippocampal granule cell neurons. Human studies also explored that impaired development of a white matter tract, in the uncinate fasciculus, in babies occurs in mothers who experienced more stress in and around the prenatal period. And it causes decreased proliferation cells in the dental dyrus of the brain and significant reduction in hippocampal granule cell neurons. Prenatal maternal depression is associated with structural changes in the amygdala. Reports showed that larger amygdala volumes are associated with behavioral disorders. Most anxiety and depression in pregnant women remain undetected and untreated during gestation. We need to make sure that pregnant women are emotionally unstable, so that the offspring are born with normal neural development.*

**Key words:** Gestation, Prenatal stress, Offspring, Behavior

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## INTRODUCTION

Gestation is an important period in a reproductive life of a female. It is a time of development of an embryo into a fetus inside the womb of the mother. A mother experiences many changes during this phase both physically as well as mentally. Stress happens to be a common feeling during pregnancy. This stress around pregnancy can result in gestational hypertension, heart diseases and even premature birth of the child. The common stress that a lady encounters are physical struggles like morning sickness, constipation, back pain and emotional instability like mood swings caused by hormonal changes. Also, psychological problems relating to personal life like negative lifetime events like death in family, divorce or loss of job, catastrophic events, depression, racism, neighborhood stress and obviously post-traumatic stress disorders also lead to gestational stress.

The early life is one of the most sensitive and essential periods during development of an individual. There has been a large body of evidence stating the association between stress during gestation and offspring's brain and behavior in both human and animals. Research that investigated maternal anxiety and depression during pregnancy have shown significant associations with emotional problems in children.

Prenatal stress activates HPA axis inducing the release of several hormones, including cortico-releasing hormone (CRH), ACTH, cortisol, and adrenaline in the bloodstream. Even smaller increase in these hormones in a pregnant mother leads to disproportionately large increases in fetal hormonal levels. These hormones have the potential to inhibit the neural growth and development [1].

Prenatal stress is associated with complications like preterm birth, preeclampsia, spontaneous abortion around gestation and post-natal effects in child with low birth weight, growth-retardation (specifically reduced head circumference) and developmental delays. It also causes heightened emotionality, externalizing behaviors, irritability and attention, cognition, and neurodevelopmental deficits [1,2].

**Studies on rodents with PNS**

Experimental evidence in rodent models support this association, showing decreased exploration in an elevated plus maze and increased reactivity to novelty in PNS-exposed rats [3]. This indicates increased anxiety-like behavior of the rats. Assessment of PNS rats with behavioral tests designed to assess depression-like phenotypes, showed an increased immobility, signifying increased depression-like behavior [4,5].

Researchers found that PNS exposed rats maintained heightened corticosterone levels with hypertrophy of the adrenal glands [6]. Furthermore, several studies explained that increased glucocorticoid levels associated with decreased negative feedback of the HPA-axis occurs after acute stress [6,7]. Another study proved that after PNS, the binding capacity of mineralocorticoid and glucocorticoid receptor were significantly decreased in PNS offspring [6-8]. The effect of stress during gestation on HPA axis activation, cognitive performance, and motor coordination was investigated along with behavioral assessments after exposure to noise stress and physical stress. Prenatal Stress resulted in anxiety-like behavior with reduced learning and memory performance and decreased motor coordination in both stressed groups compared to the controls.

**Studies on rhesus monkey**

Few research studies have examined the impact of prenatal stress on the offspring even beyond the childhood period. In this study, 7 prenatally stressed (PNS) monkeys and 7 monkeys who had undisturbed pregnancies were tested under challenging conditions at 4 years of age. Maternal separation from cage mates and their group formation resulted in PNS monkeys with more locomotion, abnormal and disturbance behavior compared to controls. PNS resulted in decreased explanatory behavior in the playroom, and distress vocalizations over time in the playroom [9].

**Underlying mechanisms proposed in PNS animal models**

Prenatal stress results in impairment of social behaviors and sensory processing with increased measures of anxiety- and depressive-like behaviours. Prenatal stress brings about persistant changes in the growth of an individual. PNS induces hypothalamic-pituitary-adrenal (HPA) axis and leads to increased anxiety-like behaviors in adult rats. Another study explained that restraint stress for chronic duration during the last week of pregnancy causes hyperphagia and impaired glucose tolerance in adult male offspring [8].

Many research that focused on identifying the mechanisms underlying the association between maternal depression and anxiety with children behaviour. An experimental evidence was assessed to evaluate prenatal stress in the form of gestational restraining procedure on hormonal/behavioral circadian rhythms. Plasma corticosterone induced by prenatal stress around gestation exhibit profound changes in circadian rhythmicity and paradoxical sleep regulation [10].

Maternal stress experienced during the last week of pregnancy markedly affects the neurogenesis in offspring. Whatever be the type of stressor repetitive restraint stress or any unpredictable stressors, offspring of both genders showed decreased proliferation cells in the dental dyrus of brain and significant reduction in hippocampal granule cell neurons [11].

Prenatal stress increases Dopaminergic D2 receptors in limbic areas, decreases DA-stimulated synthesis and release in cortical areas of brain and impairs the expression of specific transcription factors in the process of neural development [11,12].

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**Studies on human beings**

Research has found the association between maternal stress during gestation with the long-term health outcomes among offspring's in human beings as well. The impact of prenatal stress on brain starts from right from the time the child is in the womb. Not only animal studies, but even human studies have found that prenatal maternal stress affects the mental development and behavior of the offspring. Animal studies have shown that stress during pregnancy can have long lasting effects on the neurodevelopment of the offspring resulting in behavioural disorders [14].

Exposure to prenatal stress (PNS) has been associated with higher risk of affective disorders in humans as well. In humans, the association between prenatal stress and development of diverse psychosocial problems had been demonstrated in childhood and adults. Thus, the relationship between prenatal stress and cognitive, behavioral, physical, and emotional disorders like autism and attention-deficit hyperactivity disorder in children had been documented [14,15].

A research led by Di Pietro had suggested that a small degree of stress is beneficial for child outcome, with motor and cognitive development [16]. Stressful life events that occur in and around pregnancy becomes a natural disaster that poses a risk not only to maternal anxiety and depression but also increases the risk for the child towards emotional, behavioral and/or cognitive problems in future. The common disorders associated with prenatal stress are depression, anxiety, Attention Deficit Hyperactivity Disorder (ADHD), and/or conduct and other behavioural disorders, preterm delivery, and reduced telomere length [16,17].

Also, the relationship associating prenatal stress and depression and schizophrenia in adulthood, had also been explained in numerous studies. Prenatal stress affects specific regions of the brain like hippocampus, amygdala, corpus callosum, cerebral cortex, cerebellum and hypothalamus.

Another evidence proved an impaired development of a white matter tract, in the uncinate fasciculus, in babies whose mothers experienced more stress in and around the prenatal period. The mothers were made to answer a questionnaire about their experiences of stressful events and score of severity of stress was calculated. The researchers used a diagnostic method-medical imaging technique called diffusion tensor imaging to identify the structure of white matter.

Maternal exposure to stress during pregnancy is associated with increased risk for cognitive and behavioral sequelae in offspring. Another study maternal prenatal stress compared gray matter morphometry of early adolescents (11–14 years of age) and risk for problematic behaviors. PNS group exhibited increased gray matter density in bilateral posterior parietal cortex (PPC): Bilateral intraparietal sulcus, left superior parietal lobule and inferior parietal lobule. Also

then, the PS group displayed greater risk for psychiatric symptoms and dysfunction of family system dysfunction.

Another research investigated the relation between prenatal stress and child's brain and behavioral problems. A self-reported maternal pregnancy-related anxiety (PRAQ-R2 questionnaire) was collected in the second and third trimester. Voxel based morphometry analysis of brain gray matter and amydala volume was assessed. PNS resulted in pregnancy-related anxiety and child behavioral difficulties and sexually dimorphic structural changes in the limbic system of the offspring [18].

The amygdala is part of brain involved with emotions. Prenatal maternal depression is associated with structural changes in the amygdala. Reports showed that larger amygdala volumes are associated with behavioral disorders. Mostly Girls would be particularly vulnerable to such behavioural disorders [18,19].

Another study explored the potential long-term effects of prenatal exposure on the risk of schizophrenia during adulthood, as a natural experiment using the Great Tangshan Earthquake in 1976. Prenatal exposure to felt earthquake increased risk of schizophrenia compared to the unexposed [18-20].

**Possible reasons for prenatal stress related disorders**

Fetal development is process that is guided by hormones transported through placenta6. Prenatal Stress may also have an impact on the development of immune system, thereby increasing the incidence of respiratory and other infections [14].

Gestational stress can affect fetal brain development by constriction of placental arteries and reduction of fetal blood flow and oxygen supply and nutrients to brain.

In response to prenatal stress, adrenocorticotropic hormone, and aldosterone are increased in both mother and fetus. Stress Hormones like Catecholamines, corticotropin releasing hormone (CRH), and adrenal steroids penetrate the fetal brain from the maternal circulation. These hormones could produce alterations in brain structures and functions. Another explanation is that sympathetic nervous system plays a very prominent role in mobilizing energy stores during stressful conditions. PNS increased CORT levels and produces a fourfold greater effect on offspring's HPA axis.

Neuronal migration during development of embryo starts in the prenatal period and continues also towards infancy. This developmental process is an important step in formation of neuronal network. Prenatal stress exposure in the form of environmental stress, intake of alcohol, drugs, and inflammation results in disruption of neuronal migration and neuronal migration disorders and epilepsy.

## CONCLUSION

Prenatal stress had proven to have profound effects on the behavior and mental ability of a child. Most anxiety and depression in pregnant women remain undetected and untreated during gestation. We need to make sure that pregnant women are emotionally unstable, so that the offspring are born with normal neural development. Health care providers can find more implications for antenatal care. And, that regulatory role of psychosocial and genetic risk factors involved in prenatal stress is an important area in which future research should be directed.

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