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Review

The link between brain development, neonatal outcomes and maternal stress states

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ABSTRACT

Evidence shows that excessive maternal stress experienced prenatally can have detrimental short-term and long-term consequences for offspring. This is due to the link between brain development and maternal stress states. The foetus' brain goes through a series of critical developmental stages before birth. Extreme stress during the prenatal period has programming effects on the brain development. This paper explores prenatal stress and its link to abnormal behavioural, cognitive, psychosocial and socio-emotional developmental outcomes in offspring.

Introduction

During the early stages of pregnancy major neurodevelopment occurs in the foetus. These include migration of neurons, neurogenesis, proliferation, synapse formation, axonal elongation and differentiation (Davis et al., 2013; Zhu et al., 2014). The foetus cerebral endothelial junctions and blood–brain barrier forms early and is more susceptible to insults (Charil et al., 2010). The foetal brain experiences high turnover of neuronal connections and rapid growth that predicts behavioural outcomes (Davis et al., 2013).

There is evidence that excess maternal stress raises cortisol, corticotrophin releasing hormone (CRH), catecholamines and adrenal steroid levels, which reach the foetal brain from the maternal circulation. Excess of these hormones can effect the foetal brain causing reduced plasticity, neurotransmitter activity and hinder formation of neural connections in the foetal brain. This can provoke programming effects changing behaviour and cognition with the possibility of developmental delays (Lee, 2014; Thayer and Kuzawa, 2015; Weinstock, 2008). Higher maternal cortisol levels are connected with increased affective problems, mediated by the amygdala volume (Buss et al., 2012).

From reviewing current human studies, this review will clarify the effect that, high levels of maternal prenatal stress cause on behavioural, cognitive, psychosocial and socio-emotional issues in the neonate. Furthermore, it will explore the role of neonatal nurses supporting mothers with high prenatal stress and identifying preventative strategies.

Methodology

Databases used for this research paper included CINAHL, PubMed, EBSCO and Medline. Search terms included; maternal stress, brain development and neonatal/offspring outcomes with a Boolean search. Selective criteria was restricted to peer reviewed articles that were published no earlier than 2005 to ensure most current and up to date research article and evidence. 69 articles were obtained from the search and 47 were included. There is a paucity of data reporting consequences of maternal stress on offspring and the link between brain development and maternal stress.

Stress hormones

Stress is a positive or negative condition that affects your well-being, which results in the fight-or-flight response. Causes of maternal stress can be teenage pregnancy, poor mental health, pregnancy complications, stressful life events, family conflicts, exposure to violence, stressful work environment, unhealthy relationship with partner and bereavement (Henderson and Redshaw, 2016; Nur Say et al., 2016).

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When a pregnant woman is stressed, the hypothalamic-pituitary-adrenal (HPA) axis is stimulated resulting in increased production of placental cortisol and CRH (Lau, 2013; O'Conner et al., 2013; Tollenaar et al., 2011). The end product of HPA is cortisol a glucocorticoid. Maternal prenatal stress can alter the role of the HPA axis in offspring (Glover et al., 2010) as the HPA axis controls the degree of adaption and response to stressors (Maniam et al., 2014). Change in the HPA axis increases depression and anxiety in the offspring (Lazinski et al., 2008). It causes increased acetylcholine, hindering the cholinergic receptors which affects emotions, learning and memory in exposed offspring (Charil et al., 2010). Women have naturally elevated cortisol levels during pregnancy and it is fundamental for preparing the foetus for extra uterine life. Foetal exposure to abnormal increased concentrations of cortisol can change the development of neurons in the brain including growth and development (Charil et al., 2010). There is also evidence that altered cortisol levels from prenatal stress can cause distorted behavioural phenotype and depressive symptoms in adolescent girls (Glover et al., 2010; Van den Bergh et al., 2008).

Prenatal maternal stress also hinders the action of the glucocorticoid barrier enzyme, 11B-hydroxysteroid dehydrogenase type 2 (11B-HSD2) in the placenta. This leaves the foetus exposed to abnormal development and intensifies glucocorticoid exposure to the foetus. This can contribute to intrauterine growth restriction (IUGR), low birth weight (LBW), preeclampsia and preterm birth (Charil et al., 2010; Raikkonen et al., 2011). Glucocorticoids and CRH influence neuronal differentiation. Excess amounts of these hormones cause decrease in synaptic activity ion channel regulation which may result in attention and learning deficits as well as depression and anxiety (Weinstock, 2008) in the child later in life.

Glucocorticoids play a critical role in normal foetal brain development but can cause neurological consequences if too high. The brain develops early in pregnancy and has particularly vulnerable high glucocorticoid levels that are present after stress (Zhu et al., 2014). Glucocorticoid passes through the blood–brain barrier with prefrontal regions of the brain predominantly affected by excess glucocorticoids, which are involved in cognitive control (Davis et al., 2013). Exposure to excessive levels may have damaging effects on the maturation developments. Children exposed to foetal glucocorticoid have bilateral cortical thinning and the rostral anterior cingulate cortex (rACC) is proven to be thinner. Children with affective problems tend to have thinner left rACC (Davis et al., 2013). This is significant due to the rACC being involved with learning, memory and emotion formation influencing behaviour outcomes.

Excessive maternal stress in pregnancy has been shown to negatively influence the neonate's temperament (Zhu et al., 2014). Specifically, the intrauterine development can influence the neonate's neurodevelopment and temperament. This may also have consequences on the neonate's neurodevelopment throughout their entire life. A study by Lambertini et al. (2015) assessed the placenta and demonstrated the important role of mitochondria in maternal stress and neonatal temperament development. This is significant due to excess maternal stress being shown to modify mitochondria activity, causing negative temperament disorders in offspring.

Furthermore, evidence shows that excessive maternal stress during the perinatal period is associated with preterm birth and LBW (Britton, 2007; Marina et al., 2008; Van den Bergh et al., 2008; Tronick and Reck, 2009; Grote et al., 2010; Misri et al., 2010; Thompson and Fox, 2010; Insaf et al., 2011; Liou et al., 2014). LBW, preterm birth and IUGR are independently related to abnormal neurodevelopment and disabilities among children (Zhu et al., 2014; Grote et al., 2010). Exposure to increased stress during pregnancy is particularly harmful due to risks of LBW and preterm birth (Lee, 2014; Chang et al., 2014). Evidence shows that smaller size at birth and shorter gestation increases the chance of poor physical and mental health later in life and can alter HPA axis (Raikkonen et al., 2011). Elevated maternal cortisol from stress, have been associated with the development of smaller birth size (Thayer and Kuzawa, 2015; Glover et al., 2010). Preterm birth and LBW are the leading cause of infant mortality and morbidity worldwide (Lau, 2013). Maternal stress increases the risk for LBW by releasing catecholamines, which can decrease uterine perfusion. This can limit the amount of substrate delivered to the foetus and could cause reduced foetal growth (Lau, 2013).

Maternal anxiety and depression is associated with impaired social and cognitive development in offspring. Including; sleep issues, negative affection, attention-deficit hyperactivity disorder (ADHA) and emotional instability (Li et al., 2010). The prevalence of autism spectrum disorders and emotional and behaviour problems are also higher among infants of mothers with prenatal stress (Grigoriadis et al., 2013). Evidence is emerging that shows that mothers' of children with autism experienced more stressful life events during pregnancy (Kinney et al., 2008a, 2008b). Kinney et al. (2008a) found a higher prevalence of autism in children whose mothers survived severe storms or hurricanes during pregnancy, while Ronald et al. (2010) found that divorce or a residential move during pregnancy significantly increased autistic traits in two year old offspring. Autism involves dysfunction of social cognition in the brain with the orbitofrontal cortex and the amygdala playing important roles. The orbitofrontal cortex is particularly responsive to the effects of prenatal stress in the middle of pregnancy (Kinney et al., 2008a, 2008b). Prenatal stress also can change sex hormones that program sex differences in brain function and structure. This tends to be common in autistic children (Kinney et al., 2008a, 2008b).

Evidence also links experiences to stressful life events during pregnancy with behavioural and cognitive development in children (Zhu et al., 2014). Children exposed in utero to high levels of stress have shown to have less interaction with their mothers, are more irritable, difficult temperaments and exhibit poorer cognitive and play abilities (Raikkonen et al., 2011; King et al., 2009; King and Laplante, 2005). Behaviour and mental health disorders reported in offspring from maternal prenatal stress include schizophrenia, attention deficits, drug addiction, anxiety and depression (Muhammad and Kolb, 2011). These reflect impairment in the prefrontal cortical functioning (Weinstock, 2008; Glover et al., 2010). Studies have also linked maternal stress to language development and intelligence quotient (IQ) (Weinstock, 2008).

Maternal stress during pregnancy is also associated with lower cord-blood ferritin concentration. Iron is an essential component of every living cell and is particularly fundamental for early brain function. It helps glial and neuronal energy metabolism, myelination and neurotransmitter synthesis. Foetal iron deficiency relates to impaired growth and functioning of multiple organ systems, predisposes neonates to postnatal iron deficiency and contributes to long-lasting neurodevelopmental impairments. Several human studies indicate that poor perinatal iron status is associated with short-term and long-term neurological and behavioural deficits (Armony-Sivan et al., 2013; Coe et al., 2007).

Prenatal maternal stress can produce changes in placental phenotype and may effect foetal development (Eunson, 2006). It may permanently alter physiology in adulthood. Physiological alterations may result in unfavourable environment for offspring and lead to biological changes in the next generation (Lee, 2014). The reason for this is that, blood flow affects placental function. Catecholamines that are released when stressed, increase vascular resistance impacting blood flow to the placenta (Charil et al., 2010). This constriction of the placental arteries can alter placenta morphology and growth. By decreasing foetal blood flow the supply of essential oxygen and nutrients is diminished compromising

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