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Review

Effects of prenatal stress on fetal and child development: A critical literature review

R. Graignic-Philippe[a,*,1], J. Dayan[a], S. Chokron[b], A-Y. Jacquet[b], S. Tordjman[a,b,**,1]

[a] Pôle Hospitalo-Universitaire de Psychiatrie de l'Enfant et de l'Adolescent de Rennes, Université de Rennes 1 et Centre Hospitalier Guillaume Régnier, Rennes, France
[b] Laboratoire de la Psychologie de la Perception, Université Paris Descartes, CNRS UMR 8158, Paris, France

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ABSTRACT

Many studies have examined effects of prenatal stress on pregnancy and fetal development, especially on prematurity and birthweight, and more recently long-term effects on child behavioral and emotional development. These studies are reviewed and their limitations are discussed with regard to definitions (including the concepts of stress and anxiety), stress measurements, samples, and control for confounds such as depression. It appears necessary to assess individual stress reactivity prospectively and separately at each trimester of pregnancy, to discriminate chronic from acute stress, and to take into consideration moderator variables such as past life events, sociocultural factors, predictability, social support and coping strategies. Furthermore, it might be useful to examine simultaneously, during but also after pregnancy, stress, anxiety and depression in order to understand better their relationships and to evaluate their specific effects on pregnancy and child development. Finally, further research could benefit from an integrated psychological and biological approach studying together subjective perceived stress and objective physiological stress responses in pregnant women, and their effects on fetal and child development as well as on mother–infant interactions.

Contents

* Corresponding author at: Pôle Hospitalo-Universitaire de Psychiatrie de l'Enfant et de l'Adolescent (PHUPEA), 154 rue de Châtillon, 35000 Rennes, France. Tel.: +33 661 14 06 05; fax: +33 299 96 46 86.
** Corresponding author at: Pôle Hospitalo-Universitaire de Psychiatrie de l'Enfant et de l'Adolescent (PHUPEA), 154 rue de Châtillon, 35000 Rennes, France. Tel.: +33 615 38 07 48; fax: +33 299 32 46 98.
E-mail addresses: rozenn.graignic@wanadoo.fr (R. Graignic-Philippe), s.tordjman@yahoo.fr (S. Tordjman).
[1] These authors participated equally to this article.

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1. Introduction

Prenatal stress and its effects on mental and physical health are of growing interest for clinicians and researchers, as indicated by the recent literature on the subject (DiPietro et al., 2008a; Glover, 2011; Lange, 2011; O'Donnel et al., 2009; Van den Bergh et al., 2008a,b; Weinstock, 2008). Some authors suggested a direct link between mothers' emotional state, in particular perceived stress and state anxiety, and fetal or child development, including behavioral impairments (Wadhwa et al., 2001). Studies focused initially on the effects of prenatal stress on pregnancy and fetal development (mainly on birth outcomes such as birthweight and gestational length), but more recently long-term effects on child behavioral and emotional development have also been examined. Therefore, this article will consider the short-term and long-term impact of prenatal stress and review effects of prenatal stress on fetal but also child development.

Concerning effects of prenatal stress on fetal development, many studies have sought to evaluate the impact of stress on pregnancy, and in particular its relationship with prematurity and low birthweight (Class et al., 2011; Rondó et al., 2003; Roy-Matton et al., 2011). Studying the causes of prematurity and low birthweight is important given that these conditions are two of the main causes of perinatal mortality and are associated with more frequent neurodevelopmental disorders (Creasy, 1994; DiPietro, 2002). Factors of medical or obstetric risk predict only a negligible part of prematurity or low birthweight at the time of pregnancy (Shiono and Klebanoff, 1993). Certain maternal risk factors for premature delivery or low birthweight have been hypothesized in studies on prenatal stress: maternal education, mother's socioeconomic status, smoking, consumption of alcohol, young age, low weight and height before pregnancy (Aliyu et al., 2010; Da Costa et al., 1998, 2000; Gennaro, 2005; Hedegaard et al., 1993; Keegan et al., 2010; Lobel, 1994; Newton and Hunt, 1984; Olds et al., 1994; Wadhwa et al., 1993, 2001).

Effects of prenatal stress on fetal development have been studied in particular in animal models. Animal models allow the effects of a variety of stressors (Koehl et al., 1997) applied at different times of gestation to be tested (Rojo et al., 1985; Sucheki and PalermoNeto, 1991; Szuran et al., 1994), with the rat being the most common animal model studied to test the effects of prenatal stress on offspring (Barlow et al., 1978; Becker and Kowall, 1977; Henry et al., 1994; Maccari et al., 1995; Pardon et al., 2000; Peters, 1988; Politch and Herrenkhol, 1984; Power and Moore, 1986). Some studies reported effects of prenatal stress on neuronal development (Fride and Weinstock, 1989; Weinstock et al., 1988). Other studies on animal models, particularly in rats, sheep and monkeys, suggest that prenatal stress has a cause-and-effect relationship, not only with perinatal complications, such as prematurity and low birthweight, but also with long-term neurodevelopmental consequences from morphological, physiological and behavioral perspectives (Coe, 1993; Seckl, 2001; Weinstock, 2001).

The animal literature is vast and we chose to focus our literature review on human studies. However, one of the main interests of animal models is to show the importance of timing and chronicity of exposure to prenatal stress. Thus, differential effects of prenatal stress have been observed for behavioral exploration in animal models according to the period of exposure to stress during gestation. In particular, Schneider et al. (2002) reported that prenatal stress occurring during early gestation (i.e., the period of neuronal migration which might be a period of enhanced vulnerability) leads to behavioral impairments, reduced locomotion and exploration. Lordi et al. (2000) reported that when female rats were repeatedly stressed for 10 periods of 15 min by the presence of a cat, at the 10th or the 19th gestational day, the death of pups was dramatically high in the second group and, compared to controls, growth of the surviving animals was slower. Moreover, as adults, their long-term memory was altered and they exhibited aversive behavior relative to open fields and cognitive alterations, such as low levels of exploration and inability to process rapidly environmental cues. Inversely, Meek et al. (2000) observed that by 12 days old, mice pups stressed during the final week of gestation showed more exploratory behavior than did non-stressed animals. Furthermore, Rangon et al. (2007) underlined the role of chronic stress applied throughout gestation by showing that exposure of pregnant mice to chronic minimal stress throughout gestation would sensitize the offspring to neonatal excitotoxic brain lesions, which mimic lesions observed in cerebral palsy. Repeated exposure to the same stressor (restraint) in rats generated the most robust changes, including increased anxiety-related behaviors and a delayed and prolonged HPA axis response to stress in female offspring, whereas male offspring showed no change in anxiety-like behavior and had elevated basal ACTH and blunted HPA responses to stress (Richardson et al., 2006). The attenuated HPA responsivity found in male offspring is consistent with an increased negative feedback on the HPA axis (Richardson et al., 2007). Taken together, these studies suggest that the period of exposure to stress during gestation as well as its chronic occurrence may play a major role on its effects.

Finally, we chose also to focus on human studies in this article given some limitations to generalize findings from animal models to humans. As underlined by Tordjman et al. (2007), biological substrates and metabolic pathways may differ in animals and humans. Thus, cortisol is the predominant glucocorticoid in humans, whereas corticosterone is less abundant in humans (it is noteworthy that several authors reported an absence of positive association between cortisol and corticosterone among individuals; Koren et al., 2012), but is the predominant glucocorticoid in rodents. Corticosterone is the precursor molecule to the mineralocorticoid aldosterone. Corticosterone and cortisol belong to two different pathways and their regulation is mainly different (cortisol is involved in the negative feedback of the HPA axis, whereas the primary regulators of corticosterone are the renin–angiotensin system). Furthermore, the cortisol and corticosterone circadian rhythms are different within species (Albers et al., 1985) and between species (rodents are nocturnal animals and their corticosterone circadian rhythms are inverted compared to the human cortisol circadian rhythm). In addition, some manipulations and their effects in animal models are not relevant to humans. Indeed, the effects of prenatal stress on offspring studied by constraining rat females at different times of gestation are difficult to apply