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Prenatal stress and cognitive development and temperament in infants

Jan K. Buitelaar [a,*], Anja C. Huizink [a], Edu J. Mulder [b], Pascalle G. Robles de Medina [b], Gerard H.A. Visser [b]

[a] Department of Child and Adolescent Psychiatry, University Medical Center Utrecht, P.O. Box 85500, Utrecht 3508 GA, The Netherlands
[b] Department of Obstetrics, University Medical Center Utrecht, P.O. Box 85500, Utrecht 3508 GA, The Netherlands

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Abstract

Studies in rodents and nonhuman primates indicate that maternal stress during pregnancy can influence the developing fetus, resulting in delay of motor and cognitive development and impaired adaptation to stressful situations. These effects may be mediated by the hypothalamic–pituitary–adrenal (HPA) axis. We examined whether stress during pregnancy predicted developmental outcome of human infants in a prospective design. Self-report data about daily hassles and pregnancy-specific anxiety and salivary cortisol levels were collected in nulliparous pregnant women. Dependent measures were scores on the Bayley Scales of Infant Development and on temperamental questionnaires at 3 and 8 months. Pregnancy-specific anxiety in mid pregnancy predicted lower mental and motor developmental scores at 8 months. Early morning values of cortisol in late pregnancy were negatively related to both mental and motor development at 3 months and motor development at 8 months. Pregnancy-specific anxiety explained 7% of the variance of test-affectivity and goal-directedness at 8 months. Increased maternal stress during pregnancy seems to be one of the determinants of temperamental variation and delay of development of infants and may be a risk factor for developing psychopathology later in life.

Keywords: Stress during pregnancy; Fetal motor and cognitive development; HPA axis; Maternal cortisol

1. Introduction

In pregnant animals, induced stress adversely affects behavioral adaptation and motor and mental development of the offspring [41]. Stress in early or mid gestation in nonhuman primates resulted in impaired motor development, declined attention, and delayed cognitive development of offspring in the first year of life [29]. Though these findings have not yet been replicated in humans, there is increasing appreciation of the relevance of the prenatal stress paradigm for the human situation.

In ancient times, it was already a common belief that the emotional state of a mother may affect the child she is carrying [12]. Prospective studies have substantiated this belief by reporting that maternal stress during pregnancy is associated with an adverse obstetric outcome, as reflected in increased risk for premature delivery, or low birth weight for gestational age [20,23].

Recently, it was further found that prenatal stressors of human life were associated with a significantly smaller head circumference, when corrected for birth weight [20]. The aim of this paper is to review animal models on prenatal stress and to summarize our own work on the influence of prenatal stress on temperamental and cognitive development in human infants.

2. Effect of prenatal stress on behavior of rodent offspring

Aspects of development that could be influenced by prenatal stress in rodents were the early physical and motor development, exploration in a novel environment, disturbance behavior under stressful conditions, and social and sexual behaviors. Prenatal stress was associated with lower birth weights of the pups [42] and compromised early motor development [11,15]. Prenatal stress further affected the behavior of rodent offspring in a novel situation, with prenatally stressed offspring showing a decreased exploration and more defecation in an open field [15,40].

* Corresponding author. Tel.: +31-30-2508401; fax: +31-30-2505444.
E-mail address: J.K.Buitelaar@azu.nl (J.K. Buitelaar).

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Other studies, however, revealed a reverse trend, with shorter latencies to explore in the prenatally stressed rodents and more active behavior in a novel situation [10] or found no influence of prenatal stress on these behavioral measures [5]. Genetic factors might contribute to these differing results, since it was found that prenatal stress caused different offspring activity levels depending on the characteristics of their breed. For instance, two inbred strains of mice, which showed either high or low activity levels, were used to study the influence of genetic factors on the offspring response to prenatal stress. The male offspring of a low-activity strain of prenatally stressed mothers were more active than control males, whereas prenatally stressed male offspring of a high activity strain were less active. Female offspring of both strains were less active [34].

Thus, both sex effects and genetic effects seem relevant to explain different results following the exposure to prenatal stress. Environmental variables also proved to be relevant, since exploratory activity in reaction to novelty was significantly less in a bright light but not in dim light conditions [24]. In fact, in the latter condition an increase in locomotor response to novelty was observed [10].

3. Prenatal stress and behavior of nonhuman primate offspring

Prenatally stressed rhesus macaque infants had lower birth weights and compromised physical growth, and exhibited retarded motor development and shorter attention spans when compared to infants born to nonstressed mothers [28]. When tested at 6 months of age in a novel environment, the prenatally stressed infants presented with significantly more disturbance behaviors and lower amounts of exploratory behaviors compared to controls [29]. In addition, half of the prenatally stressed infants showed an abnormal response to novelty in the form of falling asleep, while none of the control infants displayed this behavior [29]. Similar effects of prenatal stress were found in pigtail macaques infants [45].

A next study tried to replicate and extend the earlier findings in three ways: squirrel monkeys were used as another primate species, repeated social stress was applied instead of noise stress, and chronic stress was contrasted to only midgestation stress and a control condition [31]. The social stress procedure involved changes in housing conditions after which the pregnant animals were exposed to unfamiliar confederates. There were no differences in birth weight between the infants from the three experimental conditions. Assessment of neuromotor functions at two weeks postpartum revealed that infants born following chronic stress were significantly behind in motor maturity and activity than the controls, with the scores of the midgestation stress infants falling in-between. Furthermore, infants from pregnancies under chronic stress maintained shorter attention spans, and had shorter durations of orienting episodes, a shorter postrotatory nystagmus and a less well developed balance control compared to controls.

Thus, the adverse influence of prenatal stress on neuromotor development could be replicated, even in the absence of an overt effect on physical growth. When the infant monkeys were examined at the average age of 18.5 months using a separation stress design, prenatally stressed infant monkeys did not differ from controls on environmental exploration or on nonsocial behavior, such as locomotion. They turned out to be different, however, in their social repertoire in that they showed more mutual clinging both in baseline and stress conditions [7]. Mutual clinging can be considered as abnormal behavior, since it is rarely observed in normally reared animals.

To examine which period of pregnancy carried the greatest vulnerability to prenatal stress in rhesus monkeys, the effects of unpredictable noise stress in early gestation were compared to that in mid-late gestation and to a nonstress condition [32]. Early gestation stress was associated with significantly lower birth weights than the mid-late gestation stress and the control condition. Further, infants born following either one of the stress conditions were clearly behind compared to the controls on measures of motor development and attention, but early gestation stress was associated with more pronounced and pervasive motor impairments than mid-late gestation stress [32]. Early rather than mid-late gestation stress was also associated with a significant decrease of activity levels. The conclusion is that sensitivity to prenatal stress in nonhuman primates peaks during early gestation and tapers off during mid-late gestation.

4. Prenatal stress and learning abilities of offspring

Studies on learning abilities of the offspring of stressed mothers have revealed impairments on a number of tasks. Early work has adduced evidence for impairments of discrimination learning [15], reversal of a learning set on a T-maze and acquisition of an operant response [33] in the offspring of prenatally stressed rats. The results of two recent studies, however, are conflicting. Using crowding combined with one daily painful experiences as stressors in Wistar rats, learning acquisition in a water-maze at day 30 did not differ between the prenatal stress and control conditions [17]. In the reversal task, however, prenatally stressed rats spent more time than control animals searching for the platform. After the application of restraint stress in Sprague–Dawley rats in the last week of pregnancy, the cognitive performance of the adult offspring (age 120 days) was tested in the water-maze and using a two-trial memory test in a Y-maze with progressive intertrial intervals [37]. Though in this design the animals showed problems in coping with novelty, expressed as an increased escape behavior, spatial learning or memory performance proved not to be affected by prenatal stress. These findings suggest that learning impairments due to prenatal stress may be present