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Spatial working memory and attention skills are predicted by maternal stress during pregnancy☆

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ABSTRACT

Introduction: Experimental evidence in rodents shows that maternal stress during pregnancy (MSDP) negatively impacts spatial learning and memory in the offspring. We aim to investigate the association between MSDP (i.e., life events) and spatial working memory, as well as attention skills (attention shifting and attention focusing), in humans. The moderating roles of child sex, maternal anxiety during pregnancy and postnatal care are also investigated.
Methods: Participants were 236 mother–child dyads that were followed from the second trimester of pregnancy until 4 years postpartum. Measurements included questionnaires and independent observations.
Results: MSDP was negatively associated with attention shifting at 18 months when concurrent maternal anxiety was low. MSDP was associated with poorer spatial working memory at 4 years of age, but only for boys who experienced poorer postnatal care.
Conclusion: Consistent with results observed in rodents, MSDP was found to be associated with spatial working memory and attention skills. These results point to postnatal care and maternal anxiety during pregnancy as potential targets for interventions that aim to buffer children from the detrimental effects of MSDP.

1. Introduction

Spatial working memory and attention skills are predicted by maternal exposure to life events during pregnancy. Research in rodents provides direct evidence of a causal role of maternal stress during pregnancy (MSDP) in spatial learning and working memory deficits in offspring [1–3]. MSDP induces alterations in the orbitofrontal and anterior cingulate cortices, two brain regions that are shared by attention and working memory [4,5]. In humans, questions remain about the involvement of MSDP in both attention and working memory. First, although some studies have found MSDP to be associated with general measures of attention [6–9], no study has yet investigated the specific aspects of attention skills that are affected, such as attention shifting and attention focusing. Second, only one study showed an association between retrospective reports of MSDP and performance in a verbal working memory task [10]. The nature of the working memory task may explain why their results are inconsistent with the observation that the spatial learning and memory deficits associated with MSDP are generally not observed in female rodents [4,11]. Whether the sex specificity of the effects of MSDP are observed in the case of spatial working memory remains to be tested.

Research in humans often investigates the mother's subjective reaction to stress (maternal anxiety during pregnancy; MADP) in addition to MSDP. In general, cognitive outcomes are more strongly associated with more objective measures of MSDP (e.g., recent life events) than MADP

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[12]. In the case of attention deficits, findings implicate both MSDP and MADP [7–9,13] while poorer working memory in offspring has only been associated with MSDP [10]. It may be the case, however, that maternal subjective anxiety modulates the association between MSDP and child outcomes. Indeed, discrepancies between objective and subjective measures of stress have been found to predict worse birth-related outcomes [15]. Moreover, MSDP is only related to poorer motor function at low levels of maternal subjective distress [14]. This raises the possibility that MADP modulates the link between MSDP and child cognitive outcomes.

Another factor that could alter the effect of MSDP on child cognitive outcome is postnatal care. Postnatal experience has been shown to moderate the association between prenatal stress and lower spatial memory performance in rodents [16]. In humans, child attachment at 18 months of age moderates the association between maternal prenatal cortisol and child cognitive development [17]. This result provides indirect evidence of the buffering role of maternal care as child attachment is strongly related to maternal care [18].

2. The current study

The main goal of the current study was to investigate the association between an objective measure of MSDP and two executive function outcomes in the child, spatial working memory and attentional skills (attention shifting and attention focusing). We then explored the role of three potential moderators: child sex, MADP and maternal care.

For this purpose, we used a sample followed prospectively from early pregnancy to early childhood. MSDP was derived from maternal exposure to stressful life events. Attention skills were measured using maternal reports, and spatial working memory was measured using a computerized assessment battery. We statistically controlled for variables that could account for the link between prenatal stress and child cognitive outcomes such as family income and child birth weight. We also controlled for maternal depression to rule out the possibility that mothers' depression explains the link between MSDP and child cognitive outcomes [19]. Finally, we controlled for maternal ratings of infant attention orienting and regulation at 6 months post partum to rule out the possibility that our results are due to maternal perceptions of child attention functioning.

3. Methods

3.1. Sample

Participants were part of the Maternal Adversity, Vulnerability and Neurodevelopment (MAVAN) study, a longitudinal study following two cohorts of mothers and their infants. For this study, we used the Hamilton, Ontario cohort, which was originally composed of 241 mothers because these mothers were recruited during the second trimester of pregnancy (weeks 12–24), whereas participants in Montreal were recruited after birth. Subjects in Hamilton were referred from the St. Joseph's Health Center (SJHC) Women's Health Concerns Clinic and SJHC Ultrasound Department, Hamilton, Ontario, Canada. Recruited mothers were 18–45 years old, most of whom reported having a partner (94%). Ethnic descent in this sample was mostly Caucasian (90%), with 3% mixed ethnicity, 2% African, 1.5% Hispanic, and 1% East Indian; the remainder were unspecified. This ethnic distribution is typical of the greater Hamilton region. The current study is based on a subsample of 236 participants because some participants were lost due to stillbirth or termination ($n = 3$) or were involved with Children's Aid Society ($n = 2$).

3.2. Procedure

Subjects signed written consent to participate in the MAVAN project. Ethics approval for this study was obtained from the ethics review boards at St Joseph's Healthcare, Hamilton, ON, and the University of Toronto, Toronto, ON. The mothers and their children started being followed during the second trimester of pregnancy (weeks 12–24). They were assessed through questionnaires, diagnostic tools and behavioral tasks. Participants received $25 compensation after each visit.

3.3. Measures

3.3.1. Demographics

Child sex, birth weight (in kilograms) and gestational age (in weeks) were used as covariates. Family income was obtained through participants reports prenatally and at 6 and 12 months postnatally. To obtain a more reliable estimate of family income, these measures were standardized and averaged (alpha = .940).

3.3.2. Maternal stress, anxiety and depressive symptoms

To obtain a relatively objective measure of maternal stress exposure, mothers reported on the number of stressful life events experienced [17]. Stressful life events during pregnancy were derived from maternal reports of life events that occurred since the beginning of pregnancy among a list 27 possible life events, including one question that allowed mothers to mention an event that had not been covered (see Appendix A). This scale was filled out during the third trimester of pregnancy. The validity of this scale is supported by its association with the Interview for Recent Life Events (IRLE), which was administered during the second trimester of pregnancy, $r = .560$. The IRLE is widely used in both clinical and research settings and has acceptable psychometric qualities [20]. However, the IRLE could not be used as a measure of MSDP because participants report on events that occurred during the previous 6 months, which meant that event happening up to 3 months before pregnancy could be reported. At 18 months postnatal, participants were administered the IRLE. Anxiety was measured using the State-Trait Anxiety Inventory [21]. Internal consistency was excellent during pregnancy and at 6 months postnatally, $\alpha = .955$ and .949, respectively. Maternal depressive symptoms were measured using the Edinburgh Postnatal Depression Scale [22]. This scale is sensitive to changes in depressive symptoms over time and can also be used in non-postnatal mothers [23]. Internal consistency was good during pregnancy and 6 months postnatally, $\alpha = .883$ and .854, respectively.

3.3.3. Maternal care

Maternal care was assessed using an observation-based measure of mother-child interaction, the Maternal Behavior Q-Sort Short Form [24,25]. Consistent with the classical definition of maternal sensitivity, it measures a mother's capacity to detect a child's signal, interpret them appropriately, and respond to them promptly and adequately. Inter-rater agreement, based on 18 independent ratings by two raters, was excellent, ICC = .940.

3.3.4. Attention skills

Early infant ability to orient their attention was measured using scales from the Infant Behavior Questionnaire at 6 months of age [26]. The global measure of attention orienting/regulation was based on a combination of 4 scales: duration of orientation, cuddliness, low intensity pleasure and soothability [26]. Internal consistency for each scale was excellent ($\alpha = .805$–.856). Based on these subscales, we created a global orienting scale. The item-total correlations were sufficiently high to justify this procedure ($rs = .338$–.630). At 18 months, mothers completed a measure of toddler temperament, the Early Childhood Behavior Questionnaire [27]. We used two scales that specifically assess attention skills at 18 months of age: attention focusing and attention shifting. Attention focusing (12 items, alpha = .798) measures the extent to which children can sustain their attention in a task and resist to distractions. Attention shifting (12 items, alpha = .631) measures the extent to which children can be flexible in the deployment of their attention or divide their attention.