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Association of prenatal maternal perceived stress with a sexually dimorphic measure of cognition in 4.5-month-old infants

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Abstract

Maternal prenatal stress can adversely impact subsequent child neurodevelopment, but little is known about its effect on cognitive development in infancy. This analysis of 107 infants from a prospective birth cohort assessed whether prenatal stress disrupts sexually dimorphic performance typically observed on a physical reasoning task. Maternal stress was assessed at 8–14 and 33–37 gestational weeks using the Perceived Stress Scale. Stress was defined as: low (scores below the median at both times), medium (scores above the median at one of the two times), and high (scores above the median at both times). At 4.5 months infants saw videos of two events: one impossible and the other possible. In the impossible event a box was placed against a wall without support underneath. In the possible event the box was placed against the wall, supported by the floor. Looking time at each event was recorded via infrared eye-tracking. Previous literature has shown that, at 4.5 months of age, girls typically look significantly longer at the impossible than at the possible event, suggesting that they expect the unsupported box to fall and are surprised when it does not. Boys tend to look equally at the two events suggesting that they do not share this expectation. This sex difference was replicated in the current study. General linear models stratified by sex and adjusted for household income, maternal education, mother's age at birth, infant's age at exam, and order of event presentation revealed that girls whose mothers reported

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

high perceived stress during pregnancy had shorter looking time differences between the impossible and possible events than girls whose mothers reported low perceived stress ($\beta = -7.1$; 95% CI: $-12.0, -2.2$ seconds; $p=0.006$). Similar to boys, girls in the highest stress category spent about the same amount of time looking at each event. For boys, there were no significant looking time differences by maternal stress level. This finding suggests prenatal stress is associated with a delay in the development of physical reasoning in girls.

Keywords

Sex differences; Maternal Stress; Cognition; Perceived Stress

1. Introduction

Recent literature has shown that maternal exposures to both chemical and non-chemical stressors during gestation are risk factors for adverse neurodevelopment. Maternal prenatal stress, a non-chemical stressor, is highly prevalent and has been associated with adverse physical and neurodevelopmental outcomes in children including lower birth weight, and impaired childhood motor and cognitive development (DiPietro, 2012; Barrett et al., 2013; Barrett et al., 2014; Kingston et al., 2015; Vehmeijer et al., 2018; Zhu et al., 2014).

When evaluating the impact of prenatal stress on cognitive development, previous studies have relied on global measures of cognition rather than measures of specific cognitive domains. The Bayley Scales of Infant Development (BSID) have been most often used, and a recent systematic review and meta-analysis of these studies found that higher maternal prenatal stress or anxiety was associated with lower scores for cognitive development on the BSID in early childhood (Kingston et al., 2015). The association of prenatal stress with child intelligence quotient (IQ) is more inconsistent, with some previous studies reporting associations of high maternal prenatal stress with poorer Full-Scale IQ scores at 7 and 11 years of age (Lamb et al., 2014) and other studies not finding consistent and statistically significant associations between IQ scores in early childhood and prenatal stress (Cortes Hidalgo et al., 2018; Laplante et al., 2008). A possible explanation for these differing results might be the different measures used to assess maternal prenatal stress and child overall cognition or the timing of cognitive assessment. For example, where IQ was assessed at older ages than the BSID, intervening experiences and development could alter the apparent association between prenatal stress and cognitive outcomes.

Maternal stress has been associated with disruptions in play behavior, an important aspect of development that is sexually dimorphic in humans (Alexander et al., 2009; Barrett et al., 2014). Barrett and colleagues (2014) showed that higher maternal stress during pregnancy was associated with a more masculinized pattern of play behavior in girls, but no significant change in boys' play behavior. These findings suggest that male and female fetuses may be differentially sensitive to maternal stress, and that prenatal stress may masculinize the play behavior of girls.

Very few human studies have assessed the effects of prenatal stress on early cognitive development and even fewer on sexually dimorphic aspects of cognition. Characterizing the

impact of prenatal stress on early cognitive development can help inform interventions to help pregnant women cope with stress thus reducing the potential for adverse impacts on the child. Such research can also identify circumstances where intervening very early in development may help to avoid adverse outcomes associated with prenatal stress. The goals of this research were to characterize the association of prenatal stress with a specific aspect of cognition measured at an earlier age than the outcomes measured in most previous studies of prenatal stress, and to examine potential sex differences in any observed associations. Our approach was unique in that it took advantage of research in developmental psychology showing that infants' looking behaviors can be used as reliable and stable measures to assess basic building blocks of cognition, in this case physical reasoning. Looking behaviors have been used to study infants' underlying cognitive processes (Aslin, 2007) by capitalizing on the fact that infants tend to look longer at stimuli that are novel or events that violate their expectations (reviewed by Baillargeon, 1995). To collect data efficiently from a large number of infants, we created an automated version of a physical reasoning task, originally designed by Baillargeon (1995), that employed infrared eye-tracking. We used this automated task to assess young infants' abilities to reason about conditions in which objects should remain in place versus when they should fall. Baillargeon's work revealed that females develop an earlier understanding than males that an object that is not physically supported should fall (at about 4–5 months of age vs. about 3–4 weeks later for males). We used this task to investigate the relationship of prenatal maternal stress, as evaluated by the Perceived Stress Scale (Cohen et al., 1988), to physical reasoning ability in male and female infants between 4 and 5 months of age.

2. Methods

2.1 Study population

The women included in this study were recruited as part of an ongoing prospective pregnancy and birth cohort study, the Illinois Kids Development Study (IKIDS) in Champaign-Urbana, IL. Women were recruited from 2014 to 2018, during their first trimester of pregnancy, from two local obstetric clinics. During their first prenatal visit, the women received a brochure with information about the study, and they filled out a card to indicate whether they were interested in learning more about the study. Women who expressed interest received a call from the IKIDS staff, during which the study was described in more detail and the woman's eligibility to participate was ascertained. Eligible women were between 18 and 40 years of age, fluent in English, not in a high-risk pregnancy or carrying multiples, living within a 30-minute drive of the University of Illinois, and not planning to move out of the area before their child reached one year of age. Women were enrolled at 8–14 weeks of gestation and provided written informed consent which included their child's participation after birth. Mothers participated in periodic study assessments across pregnancy and after the child's birth.

2.2 Prenatal Stress

The independent variable in this study was maternal perceived stress during pregnancy. Pregnant women completed the Perceived Stress Scale (PSS) (Cohen et al. 1988) two times during gestation, at 8–14 and 33–37 weeks. The PSS is a 10-item questionnaire that is used

to quantify cumulative perceived stress, by using a scale that evaluates how unpredictable, uncontrollable, and stressful respondents believe different situations in their life were during the previous month. It has been validated in multiple populations, including in pregnant women, and in a variety of countries (Baik et al., 2017; Cohen et al., 1988; Cohen et al., 2012; Khalili et al., 2017; Lee, 2012; Leung et al., 2010; Yokokura et al., 2017). Responses are rated on a five-point Likert scale ranging from 0 to 4 (0=never; 1= almost never; 2= sometimes; 3= fairly often; 4= very often). The possible total scores range from 0 to 40 with a higher total score indicating greater perceived stress. While the PSS has standard cut-offs for identifying individuals experiencing high stress, very few women in our sample met this criteria. Therefore, the median scores from women included in this analysis were used to classify the women into three stress categories: low, medium, and high. Women who scored below the cohort median at both time-points were classified as low stress. Those who scored above the median at one of the two time-points were classified as medium stress. Finally, those who scored above the median at both time-points were classified as high stress.

2.3 Physical Reasoning

To assess physical reasoning, we created an automated version of a task designed by Baillargeon (1995) in which infants watched events on a puppet stage, and their looking time was measured and recorded by hidden observers. In our automated version, infants watched computerized videos of the task on a large screen high-definition television, and their looking time was measured and recorded using an infrared eye tracker. By automating this task, it was feasible to administer it to a large sample of young infants. Study infants were assessed at 123 to 146 days of age while seated on a parent's lap in front of the television. Hereafter, we refer to this as the infant's 4.5-month visit. The testing area was surrounded by black curtains to reduce distractions. In addition, mothers wore darkened sunglasses to prevent their looking behavior or response to the videos from influencing the infant's looking behavior. Looking behaviors were tracked using an EyeLink 1000 Plus infrared eye tracker (SR Research Ltd., Mississauga, Ontario, Canada). To calibrate the eye tracker, the infant's attention was drawn to three specific calibration and validation points on the screen, using short animated clips with accompanying audio, prior to the start of the task. The infant's attention was then drawn to the center of the screen prior to each trial, to ensure that looking was not biased by gaze direction at the beginning of the trial.

The physical reasoning task assessed the infant's ability to reason about whether an object should stay in place (because it is supported), or fall (because it is not supported), and consisted of two events: a possible event and an impossible event (Figure 1). In the possible event, a gloved hand came into the scene holding a box. The hand slid the box along the floor and placed it against a wall. The hand released the box briefly, leaving it on the floor, then withdrew the box from the scene. In the impossible event, the hand placed the box against the wall, 11 inches from the floor (box height: 4.5 inches). The hand then released the box, leaving it suspended without support for 3.5 seconds before withdrawing the box. Each event lasted for about 8.5 seconds and was repeated 8 times. Thus, the impossible and possible display lasted for a total of 68 seconds each. Half of the infants saw the impossible event first and the other half saw the possible event first; the order in which infants saw the

events was randomized in blocks of 48 infants within each sex using a computerized random number generator.

Since eye-tracking allows for a fine-grained analysis of looking responses, we were able to measure infants' looking to a more constrained area than in previous studies. The interest area dimensions were of 11 by 18 inches around the perimeter of the box (Figure 1). To ensure that infants were attending to the task, we established a minimum looking time in the interest area of 7.5 seconds, which was twice the length of time the box remained in the interest area each time the glove released it. Physical reasoning ability was measured by calculating the difference in looking time between the impossible and possible events (impossible minus possible) wherein a higher value means the infant looked longer at the impossible than the possible event. At 4.5 months of age, girls typically look significantly longer at the impossible than at the possible event, suggesting that they expect the unsupported box to fall and are surprised when it does not. Boys tend to look equally at the two events suggesting that they do not share this expectation (Baillargeon, 1995). A girl's ability to detect the impossible event is believed to result from their earlier development of binocular vision allowing them to make better (more accurate) observations of events around them and learn about support relationships between objects at an earlier age, whereas binocular vision develops more slowly in males due to the actions of testosterone on the visual cortex during fetal development (Held, 1993; Held et al. 1996). Thus, this task is sensitive to sex differences in neurodevelopment.

2.4 Covariates

Study researchers met with the pregnant women three times during pregnancy. Covariate data from two of these visits to the participant's home (at 8–14 and again at 33–37 weeks) were used in this analysis and included information about key demographic, lifestyle, health, and diet variables collected via questionnaire and structured interviews. Maternal education was dichotomized to college educated versus not college educated. Household income was dichotomized at less than \$60,000 per year versus \$60,000 per year or more. Additional covariates collected included maternal smoking and alcohol consumption during the first trimester of pregnancy. At the time of the physical reasoning assessment, maternal postnatal stress was assessed with the PSS (dichotomized at the median to indicate high versus low postnatal stress), and a structured interview was used to determine whether the infant was exclusively breastfed.

2.5 Statistical Analysis

We examined descriptive and summary statistics for the relevant study variables. A Wilcoxon rank sum test was used to determine whether the expected sex difference in the outcome previously reported by Baillargeon (1995) (looking time difference between the impossible and the possible event) was replicated.

Our outcome measure was looking time difference (in seconds) defined as the impossible event looking time minus the possible event looking time. The distribution of this outcome was assessed to determine if it met the normality assumption for general linear models. General linear models were used to examine the association of prenatal maternal stress with

looking time difference. All analyses were stratified by the sex of the child given the sex difference on the physical reasoning task and the expectation that the effect of stress on the task might differ between the sexes. Regression diagnostics were performed to identify influential points, defined as observations that had extreme Cook's Distance ($D > 0.08$).

A priori knowledge and a directed acyclic graph (Hernan et al., 2000) were used to select the covariates included in the models. Socioeconomic indicators (maternal education, household income, mother's age at birth) were identified as potential confounders for inclusion in models. Infant's age at exam, and order of event presentation (impossible versus possible event shown first) were also included as covariates because they are known to be correlated with performance on the task. In addition, the interaction between order of presentation and stress was evaluated, with a criterion p-value of < 0.15 to determine whether this interaction should stay in the final model.

A number of sensitivity analyses were performed to assess the robustness of any observed associations by considering adjustment for additional covariates. Among the women in our final analysis sample ($n = 107$), there were few smokers ($n = 4$) and relatively few women reporting alcohol consumption ($n = 25$). We assessed potential confounding by smoking or alcohol in secondary analyses removing women who reported any smoking and adjusting for first trimester alcohol intake. Because of the potential for breastfeeding to be on the causal pathway, additional adjustment for breastfeeding was done as a sensitivity analysis. Sensitivity analyses were also performed retaining influential observations ($n = 1$ boy, $n = 1$ girl). Lastly, because of the correlation between pre- and postnatal perceived stress ($r_s = 0.65$ – 0.73), adjustment for postnatal stress was also done as a sensitivity analysis.

3. Results

3.1 Descriptive data

This analysis focuses on infants who participated and were age-eligible for the 4.5 month visit during two discrete periods between December of 2015 and May of 2018 when testing was conducted. A total of 193 infants were eligible to be tested. Of these infants, 162 (84%) participated in the 4.5-month visit, 123 (76%) of whom were tested; infants weren't tested if the program malfunctioned or the infant was not in the appropriate state (too fussy). A total of 114 (93% of tested infants) (57 girls and 57 boys) met criterion (minimum looking time of 7.5 seconds) on the task. Two observations identified as having high influence were removed from the analysis sample, and an additional 5 boys were missing at least one model covariate. Thus, our final adjusted analyses were performed on 56 girls and 51 boys. Table 1 details the characteristics for the 107 infants who were included in the final model. At the time of enrollment, about 86% of the mothers in the study had at least a college degree and about 69% had an annual household income of \$60,000 per year or greater. At the time of birth, women were on average 31 years of age. This subsample did not differ from the full sample of the IKIDS cohort for any of these covariates (Supplemental Table 1). Maternal smoking and alcohol consumption data were only available for the first trimester. Only 4% of our subsample reported any smoking during the first trimester and 22% reported any alcohol consumption. Women who reported drinking alcohol during the first trimester had a median of 2.5 drinks per week and none reported more than 7 drinks per week. All infants in

this subsample were born full-term (37 weeks of gestation or later). Around 64% of the infants were exclusively breastfed until the time of testing at 4.5 months of age. When stratified by sex, exclusive breastfeeding was less common in males than females. In addition, there was a tendency for mothers of male infants to be less educated (Table 1).

3.2 Maternal Stress

The median maternal PSS score at 8–14 weeks of gestation was 11 with a range from 0 to 36. At 33–37 weeks of gestation, the PSS median score was 10 with a range from 0 to 27. Prenatal stress scores at the two time points were moderately correlated ($r_s = 0.64$).

Although, the prevalence of high maternal prenatal stress was similar in mothers of female and male infants, the distribution of low and medium level prenatal maternal stress varied by infant sex (Table 1). However, these were not statistically significant differences. In addition, mothers of male infants had lower postnatal perceived stress compared with mothers of female infants (Table 1). The median postnatal PSS score was 9 with a range from 0 to 35. Prenatal stress scores at both time points were highly correlated with postnatal stress scores ($r_s = 0.73$ and $r_s = 0.65$, respectively).

3.3 Physical Reasoning Task

Among the 107 infants in the analysis, the mean (range) looking time for the impossible event in girls was 21.5 (7.6–44.1) seconds and in boys was 19.2 (7.5–36.7) seconds and for the possible event in girls was 17.8 (7.5–35.1) seconds and in boys was 18.4 (7.6–32.4) seconds. As expected, the Wilcoxon rank sum test showed that the difference in looking time between the two events (impossible minus possible) was higher among girls than boys. Girls, on average, looked at the impossible event 3.7 seconds longer than the possible event, whereas, in boys the difference in looking time was 0.8 second ($p = 0.04$) (Figure 2).

There was no evidence of a significant ($p < 0.15$) interaction between order of event presentation and stress so this interaction was not included in multivariable models. In covariate-adjusted general linear models stratified by sex, girls whose mothers had higher levels of perceived stress during pregnancy had significantly shorter looking time differences than girls whose mothers had low levels of perceived stress ($\beta = -7.1$; 95% CI: $-12.0, -2.2$ seconds; $p = 0.006$). There was a similar trend comparing girls whose mothers had medium versus low perceived stress ($\beta = -3.4$; 95% CI: $-8.5, 1.6$ seconds; $p = 0.18$). The covariate-adjusted mean $\pm$ SE looking time difference for girls was 7.1 ± 2.8 seconds in the low stress group ($n = 17$), 3.7 ± 2.4 seconds in the medium stress group ($n = 18$), and 0.3 ± 2.1 seconds in the high stress group ($n = 21$) (Figure 3). In addition, there was a significant main effect of maternal age at birth, with girls looking slightly longer at the impossible event with each year of increasing maternal age ($\beta = 0.7$; 95% CI: $0.1, 1.3$ seconds; $p = 0.02$). In boys, there was no association of prenatal stress with looking time difference but there was a significant main effect of the order of events ($p = 0.0007$); boys looked longer at whichever event they saw first regardless of whether it was the possible or impossible event.

3.4 Sensitivity Analyses

Findings were essentially unchanged when we excluded infants whose mothers reported smoking during the first trimester ($n = 4$), or when we adjusted models for maternal alcohol

consumption during the first trimester or breastfeeding status at the time of exam. In addition, inclusion of the two influential observations in our models did not materially alter findings. When adjusting for postnatal maternal stress, associations with prenatal maternal stress were attenuated with wide confidence intervals, but girls whose mothers had higher levels of perceived stress during pregnancy still had shorter looking time differences than girls whose mothers had low levels of perceived stress ($\beta = -3.9$; 95% CI: $-10.4, 2.6$ seconds; $p=0.23$). The difference between girls whose mothers had medium versus low perceived stress was also attenuated and imprecise ($\beta = -1.3$; 95% CI: $-7.1, 4.5$ seconds; $p=0.65$). Similar to associations with prenatal stress, girls whose mothers had higher perceived stress postnatally showed shorter looking time differences than girls whose mothers had low levels of perceived stress postnatally ($\beta = -4.0$; 95% CI: $-9.5, 1.4$ seconds; $p=0.14$). As was the case for prenatal stress, maternal postnatal stress was not associated with differences in looking time in boys.

4. Discussion

Our results replicated the findings of sex difference in physical reasoning reported by Baillargeon (1995) among 4.5-month-old infants. Girls on average looked significantly longer at the impossible event, suggesting this event violated their expectations. Whereas boys did not have a significant difference in looking time, suggesting they do not share this expectation yet. This result demonstrates that an automated version of the task, using a computerized video display and an eye-tracking system, produced results very similar to those obtained with the live, puppet stage version that had been used previously. This automated approach has several advantages. It allows efficient testing of large numbers of infants, yields high quality quantitative data, and requires little training to administer, making this approach ideal for epidemiological settings.

Given previous literature on the association of maternal stress during pregnancy and sexually dimorphic outcomes, we hypothesized that higher prenatal maternal stress would be associated with sex-specific changes in girls' performance on the physical reasoning task. Our results show that the association between prenatal maternal perceived stress and physical reasoning differs by infant sex. Girls exposed to high levels of prenatal maternal perceived stress did not show the expected difference in looking time and looked at the impossible and possible events for about the same time, suggesting a delay in the development of physical reasoning regarding object support. Furthermore, this is reflective of slower cognitive development. In contrast, boys did not show an association between prenatal maternal perceived stress and looking time difference. This result could be due to a sex difference in susceptibility to prenatal stress, however, it could also be related to developmental timing. Boys are expected to develop an understanding of object support about a month later than girls. Hence, we cannot rule out that there could be an effect of stress in infant boys if they had been assessed at a later age.

The results presented are consistent with previous studies examining the association between prenatal stress and sexually dimorphic aspects of development. Barrett et al. (2013 and 2014) studied the effects of prenatal maternal stress on both physical and behavioral aspects of development. They assessed stress using a Stressful Life Events scale, which asks about

stressful events that might have happened during pregnancy, such as loss of a job or relationship difficulties. At 12.6 months of age the anogenital distance (AGD) was assessed in the offspring of enrolled mothers. This has been shown to be a good biomarker of androgen exposure. Normally, males have a longer AGD than females. Results showed that females whose mothers were exposed to more life event stressors had a longer AGD than females whose mothers had fewer stressful events during pregnancy. At 4 & 5 years of age, the same cohort of children were evaluated with the Preschool Activities Inventory (PSAI) to assess play behavior. Results showed that females whose mothers had higher life event stressors during pregnancy had more masculinized play behavior than females whose mothers who reported no stressors. These two findings are consistent with our results on the physical reasoning task. There is evidence to indicate that all three outcomes (AGD, play behavior, and our physical reasoning task) are mediated by exposure to androgens during development (Barrett et al., 2013; Barrett et al., 2014; Held, 1993; Held et al. 1996). Even though the underlying mechanisms of stress's impact on neurodevelopment are unknown, Barrett and colleagues (2013) suggest that maternal prenatal stress might induce increases in fetal cortisol and consequent increases in fetal testosterone (produced by either the placenta or the fetus).

Our findings support the possibility that postnatal stress might explain some of the observed difference in physical reasoning. Similar to prenatal stress models, girls exposed to higher levels of postnatal maternal perceived stress had a significantly shorter looking time difference than girls in the low postnatal stress category. However, in our analysis, it was difficult to differentiate associations with pre- and postnatal stress since the two were highly correlated ($r_s = 0.65-0.73$). To differentiate prenatal and postnatal effects, a much larger sample size would be needed to identify sufficient numbers of women with high levels of prenatal stress only, high levels of postnatal stress only, or both.

It is important to mention that our study population had relatively low levels of stress overall compared to nationally representative scores in U.S. women reported by Cohen and colleagues in 2012. Our sample had mean (SD) PSS scores of 11.5(6.1) at 8–14 weeks of gestation and 10.6 (6.4) at 33–37 weeks of gestation. Cohen and colleagues (2012) reported that females in their sample in 1983 had a mean (SD) PSS score of 13.7 (6.6) ($n=1,344$), in 2006 of 16.1 (7.7) ($n=1,034$), and in 2009 of 16.1 (7.6) ($n=1,032$). They also reported that participants' PSS scores decreased with increasing education and income. The relatively low scores in our IKIDS sample may be related, at least in part, to the study population's high levels of education and income.

There are some limitations to the current study. One limitation is the small sample size, which limits the ability to address issues such as the impact of pre-versus postnatal maternal stress. Another limitation is that we only had smoking and alcohol data for the first trimester of pregnancy. However, only four women reported smoking during the first trimester, and it is unlikely women would start smoking later in pregnancy. The subset of women who reported consuming alcohol reported a median of 2.5 drinks per week and this alcohol intake was not correlated with stress nor with looking time differences; therefore, it is unlikely that alcohol intake during pregnancy would confound observed associations and sensitivity analyses adjusting for alcohol confirmed this conclusion. There are potential concerns that

the present analysis relied on perceived stress and we did not have biological measures of stress. However, a positive correlation between PSS score and biomarkers of cortisol has been observed in some studies (Bowers et al., 2018; Kalra et al., 2017) thereby supporting the value of PSS as a proxy indicator of physiological stress response. There are two other concerns related to the PSS. First, we categorized stress levels based on our sample scores on the PSS, this means our specific stress categories may not be generalizable to other populations. That said, finding changes in performance on an infant physical reasoning task associated with relatively low levels of maternal perceived stress (the average PSS score in our high stress group was 16.5) is still a broadly applicable observation. Also, the PSS does not capture other potentially relevant domains including depression, anxiety and life event stressors so there is likely some measurement error in our categorization of stress exposure.

In conclusion, our results suggest that maternal perceived stress is associated with poorer physical reasoning in girls, but not boys, at 4.5 months of age. Our findings provide additional evidence that maternal prenatal stress can impact early neurodevelopment, and together with previously reported findings, suggest that females may be more sensitive to the effects of maternal stress than males.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Results replicated the findings of sex difference in physical reasoning reported by Baillargeon (1995) among 4.5-month-old infants.
- Results show that the association between prenatal maternal perceived stress and physical reasoning differs by infant sex.
- Girls exposed to high levels of prenatal maternal perceived stress did not show the expected difference in looking time in the physical reasoning task. In contrast, boys did not show an association between prenatal maternal perceived stress and looking time difference.

Figure 1. Physical Reasoning Task consists of two video events, the possible (top) and the impossible (bottom) event. The orange squares encompass the interest area used to identify infants who are looking at the box.

Figure 2. Sex stratified mean (SE) looking time differences on a physical reasoning task in IKIDS 4- to 5-month-olds (*p-value=0.04).

Figure 3.

Adjusted least squares means of looking time differences (SE) on a physical reasoning task by prenatal stress exposure. Results stratified by sex in IKIDS 4.5-month-olds (n=107).

There was a significant difference between girls in the low and high stress groups ($p=0.02$).

Table 1

Overall and sex stratified demographic and lifestyle characteristics of IKIDS mother-infant pairs participating in infant physical reasoning assessments

	Subsample (n=107)		Girls (n=56)		Boys (n=51)	
	N (%)	Mean (SD)	n (%)	Mean (SD)	n (%)	Mean (SD)
Maternal race						
White, Non-Hispanic	88 (82)		44 (79)		44 (86)	
Other	19 (18)		12 (21)		7 (14)	
Maternal age (years)		30.9 (3.9)		30.7 (3.6)		31.2 (4.2)
Maternal education						
Some college or less	15 (14)		4 (7)		11 (22)	
College degree or higher	92 (86)		52 (93)		40 (78) *	
Annual household income						
<\$60,000	33 (31)		17 (30)		16 (31)	
>= \$60,000	74 (69)		39 (70)		35 (69)	
Maternal smoking (first trimester)	4 (4)		1 (2)		3 (6)	
Maternal drinking (first trimester)	24 (22)		10 (18)		14 (27)	
Mode of delivery (% cesarean)	21 (20)		9 (16)		12 (24)	
Gestational age (weeks)		39.5 (1.2)		39.6 (1.2)		39.3 (1.1)
Infant age at time of testing (months)		4.4 (0.20)		4.4 (0.20)		4.4 (0.21)
Feeding status¹						
Exclusively breastfed	68 (64)		46 (82)		22 (43) *	
Other	39 (36)		10 (18)		29 (57)	
Prenatal Maternal Stress (category)²						
Low	39 (36)		17 (30)		21 (41)	
Medium	28 (26)		18 (32)		10 (20)	
High	41 (38)		21 (38)		20 (39)	
Postnatal Maternal Stress (category)³						
Low	52 (49)		22 (39)		30 (59) *	
High	55 (51)		34 (61)		21 (41) *	

¹ Feeding status at the time of the 4.5-month evaluation. Feeding status of "Other" includes infants that were exclusively formula fed and infants that had both formula and breastmilk.

² Prenatal maternal stress was assessed using the 10-item Perceived Stress Scale at 8–14 and 33–37 weeks of gestation. Categories were defined as: low (scores below the median at both times), medium (scores above the median at one of the two times), and high (scores above the median at both times).

³ Postnatal maternal stress was assessed using the 10-item Perceived Stress Scale at the 4.5-month visit. Categories were defined as: low (scores below the median) and high (scores above the median).

* Bold values represent significant statistical difference between girls and boys.