# Maternal Life Stress Events in Pregnancy Link to Children's School Achievement at Age 10 Years

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**Objective** To test the hypothesis that maternal antenatal exposure to life stress events is associated with lower achievement in literacy and numeracy at age 10 years, with sex differences in this link.

**Study design** The Western Australian Pregnancy Cohort Study recruited 2900 women at 18 weeks' pregnancy, and 2868 children were followed up at birth and postnatally. At age 10 years, information on 1038 children was linked to their literacy and numeracy test scores. Multivariate regression models were used to test the foregoing hypotheses, adjusting for important confounders.

**Results** In girls, maternal antenatal exposure to 4 or more maternal life stress events or death of the mother's friend and/or relative was associated with lower reading scores. In contrast, exposure to 3 or more life stress events or to a pregnancy or financial problem was associated with higher reading scores in boys. Furthermore, maternal exposure to 4 or more life stress events was associated with higher mathematic scores and a residential move was linked to higher writing scores in boys.

**Conclusion** Maternal antenatal exposure to life stress events has differing effects on the school performance of male and female offspring. Further research is needed to explore the reasons for this sex difference. *(J Pediatr 2013;162:483-9)*.

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A substantial body of evidence has linked maternal stress during pregnancy to difficult infant temperament,[1-3] child behavioral problems,[4-9] and attention deficit hyperactivity disorder symptoms in children aged 4-15 years.[4,10] Other studies also have reported a negative effect of maternal stress in pregnancy on cognitive development.[1,3,11,12]

Previous studies linking maternal stress in pregnancy to child cognitive development have been based mainly on small study samples (<100 participants) and focused on infants, toddlers, or young children. However, middle childhood and adolescence are important developmental stages, at which individual cognitive capabilities become more differentiated and stabilized.[7] It is also at this developmental stage that self-regulatory capacities (ie, executive functions) begin to develop, and they mature throughout the teenage years.[13,14] Indeed, several studies have linked maternal stress in utero to cognitive function in middle childhood and adolescence.[4,15,16]

A child's numeracy and literacy achievements are important outcome measures of cognitive development, with significance for the individual's capability to participate successfully in society later in life. Consequences of low educational achievement include low self-esteem, social, emotional and behavioral problems, early school dropout, unemployment, and ultimately poverty,[17] with a risk of an intergenerational transmission of disadvantage.[18,19] To date, only one study has examined the link between maternal stress events in pregnancy and academic performance.[20] Niederhofer and Reiter[20] examined the association between the occurrence of any of 26 self-reported maternal stress events between 16 and 20 weeks' gestation in 227 women in Vienna, Austria and fetal movement (measured by ultrasound imaging), followed by evaluation of child temperament at age 6 months and teacher-reported marks on literacy, numeracy, and music at age 6 years. The findings revealed that maternal antenatal stress events related to socioeconomic issues (eg, financial problems) and psychological factors (eg, isolation) were associated with lower marks in all 3 of these areas.

A range of animal studies has demonstrated sex differences in the effects of maternal psychological stress during pregnancy on behavioral and cognitive outcomes in offspring.[21] Previous research in humans suggests that the female fetus is more sensitive to changes in placental cortisol concentrations resulting in growth alterations.[22] Female children and adolescents affected by Hurricane Katrina in the US in 2005 reported higher levels of depressive symptoms and

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|---|---|
| WALNA | Western Australian Literacy and Numeracy Assessment |

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posttraumatic stress disorder than their male counterparts.[23,24] These sex differences may be attributed to genetic variability within the stress regulatory systems,[25,26] suggesting possible sex differences in the effect of maternal exposure to life stress events during pregnancy on numeracy and literacy skills of offspring.

The present study examined the relationship between maternal exposure to common life stress events during pregnancy and children's subsequent achievement in numeracy, reading, spelling, and writing in children from the relatively large Western Australian Pregnancy Cohort (Raine) Study who had reached age 10 years and attended grade 5 in the Australian primary school system. We hypothesized that: (1) maternal exposure to life stress events during pregnancy was negatively associated with academic achievement at age 10 years, independent of maternal social and demographic characteristics, maternal smoking during pregnancy, family income, and life stress events at age 10 years; and that (2) maternal exposure to life stress events during pregnancy would have different effects on academic achievement in boys and girls at age 10 years.

## Methods

The study was based on longitudinal data from the Raine Study, a prospective cohort study of 2868 live births with ongoing follow-up. Between 1989 and 1991, the Raine Study recruited 2900 pregnant women through the state maternity hospital (King Edward Memorial Hospital) and nearby private clinics in Perth, Western Australia. These women were recruited between 16 and 20 weeks' gestation, with sufficient English language skills, and an intention to give birth at King Edward Memorial Hospital and to reside in Western Australia to allow follow-up.[27]

Participants provided data on their pregnancy, maternal physical health, maternal experience of common life stress events, and psychosocial and demographic characteristics at enrollment and at 34 weeks' gestation. The primary caregiver (usually the mother) and the child were followed up at birth and at age 1, 2, 3, 5, 8, 10, 14, and 17 years. The primary caregiver provided informed consent at enrollment and at each subsequent follow-up after birth. The study was approved by the Human Research Ethics Committees at King Edward Memorial Hospital and Princess Margaret Hospital for Children, Perth.

This study was based on a subset of the Raine cohort at age 10 years. These children (n = 1038: 521 boys and 516 girls) were in grade 5 in government schools and were linked to the data from the Western Australian Literacy and Numeracy Assessment (WALNA) conducted by the Western Australian Department of Education and Training. These children represent about 51% of the cohort that was followed up at age 10 years (n = 2047). Compared with the children who were followed up at age 10 years but not linked to WALNA, these children were less likely to be born to a teenage mother ($P < .001$) or a mother who never married ($P = .05$), or to a family with an annual income below $AUD 36 000 in 1989-1991 ($P = .02$), with absolute differences of approximately 4 percentage points. There was no difference in maternal education between the 2 groups ($P = .70$). Children who attended nongovernment schools were not included in this data linkage, because additional permission and consent from the Independent Schools' Association could not be obtained at the time. The WALNA and Raine datasets were linked by the Western Australian Data Linkage System using a probabilistic method of matching based on full names, date of birth, sex, and address, as described elsewhere.[28]

### Numeracy and Literacy Assessment at Age 10 Years

Standardized scores were derived from raw test scores for mathematics, reading, writing, and spelling, obtained through the WALNA, which is administered annually to all Western Australian students in grades 3, 5, and 7. The WALNA is directly comparable with other Australian statewide assessment programs of child school achievement, and is evaluated annually for content and construct validity by psychometricians.

The raw scores were standardized based on a historical scale developed by the Western Australia Department of Education and Training to enable comparisons over time. These scores were converted from an ordinal scale into an interval scale using a Rasch measurement model[29] to enable easier interpretation and allow for monitoring of children's progress in literacy and numeracy skills over time. The interval scale measures the levels of achievement in mathematics, reading, writing and spelling, with higher scores indicating higher levels of achievement.

### Stress Events in Pregnancy

Each pregnant mother completed a questionnaire at 18 weeks' and again at 34 weeks' gestation, which asked whether or not she had experienced any of 11 life stress events: pregnancy problems, death of a close friend or relative, separation or divorce, marital problems, problems with other children in the family, own job loss (involuntary), partner's job loss (involuntary), financial problems, residential move, and other stressful events. At 18 weeks' gestation, the mother was asked whether she had experienced any of these life stress events since becoming pregnant, and at 34 weeks' gestation, she was asked whether any of these stressful events occurred since 18 weeks' gestation. Possible answers to these questions were dichotomous ("yes"/"no") to reduce recall difficulties and bias.[30]

We adopted the scale developed by Miller and Rahe[31] to weight the 11 stress events according to severity, with the death of a relative having the greatest weight (96) and residential move the lowest (41). The total weighted score sums all life stress events experienced at both 18 weeks' and 34 weeks' gestation. If a mother reported a total of 3 different life stress events (eg, death of a close relative, separation or divorce, residential move) at both time periods, her total weighted score would be 92 + 79 + 41 = 212, and the weighted average score for her pregnancy would be 212/2 (time periods) = 106; we used the weighted average score in our analyses. In addition, we examined the following 3 aspects of exposures to life stress events during pregnancy to provide a more nuanced view of the effect of antenatal stress exposure on children's learning outcomes.

A total life stress events index score was derived by summing the number of "yes" responses to any of the 11 life stress events throughout the pregnancy, giving equal weight to each and excluding missing cases (7%; n = 74). Preliminary analysis suggested that the number of the life stress events had a nonlinear association with the outcome variables; thus, we collapsed the total number of life stress events into 4 categories: no life stress event, 1 or 2 life stress events, 3 life stress events, and 4 or more life stress events.

We classified the timing of life stress events during pregnancy into 4 categories: no stress events in pregnancy (reference group), life stress events in early pregnancy only (up to 18 weeks' gestation), life stress events in midpregnancy only (between 19 and 34 weeks' gestation), and life stress events in pregnancy up to 34 weeks' gestation. We also examined whether the mother had experienced each of the 11 life stress events ("yes"/"no") at any time during pregnancy.

### Confounding Variables

Many of the life stress events under investigation are closely associated with or caused by social and economic disadvantages, such as marital problems, involuntary job loss, money problems, and residential mobility.[32] To control for these possible confounders, our multivariate analyses included maternal age (<20, 20-24, 25-29, 30-34, and ≥35 years), education (no schooling, trade certificate/other qualification type/college diploma, professional degree, and university degree), marital status (married, never married/de facto, separated/divorced, or widowed), and race (Aboriginal, Caucasian, other), along with family income ($AUD <24 000, 24 000-35 999, or ≥36 000) and the average number of cigarettes the mother smoked daily at 18 weeks' gestation (0, 1-5, 6-10, 11-15, 16-20, and 21 or more). Furthermore, because several maternal life stress events during pregnancy can persist in infancy and up to age 10 when literacy and numeracy testing was performed, the life stress events at these 2 later developmental stages were a plausible confounder. To adjust for this factor, all of our multivariate analyses included a weighted scale of stress events at age 1 year and 10 years, using the same weighting scale for the life stress events reported during pregnancy.

### Statistical Analyses

We tested for main effects and sex interactions with each measure of maternal exposure to life stress events, with adjustment for the confounders. Analyses were done using multivariate general linear regression models in SPSS version 16 (SPSS, Chicago, Illinois). The sex interactions were tested by including interaction terms (eg, sex*weighted_stress) along with other covariates and a request for marginal means in the model statement. The term "effect" was used in a statistical context and was interchanged with the term "association," without the intention to claim full causality. An effect of $P \leq .05$ was considered statistically significant, with due attention to overall patterns and the magnitude of the effect where the $P$ value was ≤.10.

## Results

Compared with girls, boys had a higher average score for mathematics, but lower scores for all 3 measures of literacy (Table I). There were considerable sex differences in the average scores of reading ($P$ = .049), spelling ($P$ = .01), writing ($P \leq .001$), and numeracy ($P$ = .069). The SD in numeracy outcomes was larger in boys than in girls, but the opposite held true for spelling and writing outcomes.

On average, the mothers of the Raine Study cohort subset experienced 2 stress events during pregnancy (Table II). Nearly 80% experienced at least one stress event sometime during pregnancy, and in 42.7% a life stress event occurred at both 18 weeks' and 34 weeks' gestation. The most commonly reported life stress events were pregnancy problems (37.4%), followed by money problems (35.5%), residential move (25.4%), other problems (21.5%), and marital problems (11.9%). On the weighted scale, the mean score of total stress exposure was 59.7, with a minimum of 0 and a maximum of 352.

### Reading

Overall maternal life stress events in pregnancy had a negative effect on girls' reading test scores but a positive effect on boys' scores independent of the potential confounders (Table III): for every 1 unit increase in the stress scale, the reading score decreased by 0.18 point in girls but increased by 0.17 point in boys. The sex difference is statistically significant (beta = −0.27; 95% CI, −0.50 to −0.04; $P$ = .023). When a weighted stress scale for the life stress events at age 1 year was added to the multivariate models, the negative effect in girls decreased only somewhat (from beta = 0.18 to beta = 0.17) even though the statistical significance was reduced from $P$ = .04 to $P$ = .08. For boys, the positive effect on reading increased, from beta = 0.17 to beta = 0.21 ($P$ = .05 to $P$ = .02).

Girls whose mother experienced 4 or more life stress events scored approximately 33 points lower on the reading test compared with the reference group (no stress events)

**Table I.** Average numeracy and literacy scores at age 10 years by sex

| | All (n = 1038), mean ± SD | Boys (n = 521), mean ± SD | Girls (n = 516), mean ± SD | Difference in mean | *P* value | 95% CI |
|---|---|---|---|---|---|---|
| Math | 397 ± 106 | 403 ± 111 | 391 ± 101 | 12 | .069 | −24.87 to 91.49 |
| Reading | 384 ± 104 | 378 ± 104 | 391 ± 104 | −13 | .049 | 0.064 to 25.38 |
| Spelling | 361 ± 119 | 348 ± 146 | 375 ± 190 | −27 | .011 | 6.22 to 47.38 |
| Writing | 423 ± 169 | 409 ± 116 | 437 ± 121 | −28 | <.001 | 13.98 to 42.91 |

**Table II. Maternal experience of life stress events in pregnancy**

| | All (n = 964) | Boys (n = 486) | Girls (n = 478) |
|---|---|---|---|
| Total number of stressful events, mean ± SD (range) | 2.09 ± 1.90 (0-11) | 2.13 ± 1.92 (0-10) | 2.06 ± 1.89 (0-11) |
| Weighted total stress events, mean ± SD (range) | 59.7 ± 55.3 (0-352) | 60.5 ± 5.7 (0-319) | 58.7 ± 55.0 (0-352) |
| Frequency of exposure to stress events, n (%) | | | |
| No stressful events | 206 (21.4) | 101 (20.8) | 105 (22.0) |
| 1 stressful event | 244 (25.3) | 119 (24.5) | 125 (26.2) |
| 2 stressful events | 178 (18.5) | 96 (19.8) | 82 (17.2) |
| 3 stressful events | 146 (15.1) | 76 (15.6) | 70 (14.6) |
| 4 or more stressful events | 190 (19.7) | 94 (19.3) | 96 (20.1) |
| Timing of exposure, n (%) | | | |
| No stressful events | 206 (21.4) | 101 (20.8) | 105 (22.0) |
| Stress events at 18 weeks' gestation | 215 (22.3) | 103 (21.2) | 112 (23.4) |
| Stress events at 34 weeks' gestation | 131 (13.6) | 66 (13.6) | 65 (13.6) |
| Stress events at 18 and 34 weeks' gestation | 412 (42.7) | 216 (44.4) | 196 (41.0) |
| Specific life stress events 18 and 34 weeks' gestation, n (%) | | | |
| Death of a friend | 33 (3.4) | 14 (2.7) | 19 (3.6) |
| Death of a relative | 86 (8.9) | 38 (7.4) | 48 (9.2) |
| Pregnancy problems | 361 (37.4) | 188 (36.4) | 173 (33.2) |
| Personal job loss | 34 (3.5) | 18 (3.5) | 16 (3.1) |
| Partner's job loss | 78 (8.1) | 37 (7.2) | 41 (7.9) |
| Separation or divorce | 43 (4.5) | 25 (4.8) | 18 (3.5) |
| Marital problem | 115 (11.9) | 55 (10.7) | 60 (11.5) |
| Residential move | 245 (25.4) | 116 (22.5) | 129 (24.8) |
| Money problem | 342 (35.5) | 177 (34.3) | 165 (31.7) |
| Problem with children | 102 (10.6) | 48 (9.3) | 54 (10.4) |
| Other problems | 204 (21.2) | 96 (18.6) | 108 (20.7) |

(**Table III**). In contrast, in boys, maternal exposure to 3 or more life stress events was associated with an approximate 41-point increase in the reading test score. The sex interaction with the frequency of exposure to life stress events was statistically significant ($P = .02$; $F = 3.12$; df = 3), after adjusting for maternal age, race, marital status, education, smoking in pregnancy, family income, and a weighted stress scale at age 1 year and 10 years (**Figure**). The mean reading score for girls did not differ between no stress events and 1-2 stress events (~401 vs 402), but it decreased slightly at 3 stress events (400), and more substantially when mothers were exposed to 4 or more

**Table III. Effects of maternal experience of stressful events in pregnancy on WALNA reading test scores at age 10 years**

| | Girls | | | Boys | | |
|---|---|---|---|---|---|---|
| | Beta | *P* value | 95% CI | Beta | *P* value | 95% CI |
| Weighted scale of total stress exposure | −0.18 | .04 | −0.35 to 0.01 | 0.17 | .05 | −0.002 to 0.34 |
| Weighted scale of total stress exposure adjusting for stress exposure at age 1 year | −0.17 | .07 | −0.35 to 0.01 | 0.21 | .02 | 0.04 to 0.39 |
| Frequency of exposure to stress events* | | | | | | |
| No stress events (reference) | - | - | - | - | - | - |
| 1-2 stressful events | −0.09 | 1.0 | −25.28 to 25.11 | 22.08 | .06 | −1.12 to 45.28 |
| 3 stressful events | −4.73 | .78 | −34.47 to 28.02 | 41.23 | <.01 | 11.37 to 71.09 |
| 4 or more stressful events | −33.27 | .03 | −64.04 to −2.51 | 40.52 | <.01 | 10.83 to 70.21 |
| Timing of exposure* | | | | | | |
| No stress events (reference) | - | - | - | - | - | - |
| Stressful events at 18 weeks' gestation | −4.36 | .76 | −32.92 to 24.19 | 25.03 | .07 | −1.87 to 51.92 |
| Stressful events at 34 weeks' gestation | 11.52 | .50 | −21.86 to 44.91 | 24.89 | .11 | −5.94 to 55.71 |
| Stressful events at 18 and 34 weeks' gestation | −18.38 | .17 | −44.56 to 7.80 | 32.72 | <.01 | 8.30 to 57.18 |
| Specific stress events at 18 and 38 weeks' gestation*,† | | | | | | |
| Death of a friend | −97.24 | <.001 | −151.40 to −43.09 | −5.41 | .82 | −52.11 to 41.29 |
| Death of a relative | −35.12 | .05 | −70.43 to 0.19 | 9.08 | .55 | −20.52 to 38.68 |
| Pregnancy problem | −4.54 | .65 | −23.93 to 14.85 | 21.47 | .02 | 3.16 to 39.77 |
| Personal job loss | 33.27 | .19 | −17.04 to 83.58 | 13.65 | .59 | −36.06 to 63.36 |
| Partner's job loss | −3.29 | .86 | −39.01 to 32.42 | 25.23 | .11 | −5.89 to 56.34 |
| Separation or divorce | −38.51 | .12 | −86.61 to 9.59 | −14.10 | .60 | −37.16 to 65.34 |
| Marital problem | −24.92 | .12 | −56.00 to −6.17 | 7.24 | .63 | −21.85 to 36.34 |
| Residential move | 12.43 | .29 | −10.43 to 35.28 | −3.10 | .77 | −17.79 to 24.00 |
| Money problem | −4.69 | .67 | −25.93 to 16.56 | 27.01 | .01 | 7.18 to 46.92 |
| Problem with children | −10.43 | .54 | −43.87 to 23.00 | 12.47 | .39 | −16.07 to 41.01 |
| Other problems | −11.92 | .33 | −36.11 to 12.27 | 3.12 | .77 | −17.93 to 24.18 |

*Each indicator of the stress event was analyzed in a separate multivariate model that adjusted for maternal age, race, marital status, education, smoking in pregnancy, family income, and a weighted stress scale at both age 1 year and age 10 years.
†The reference group was no exposure to a specific stressful event.

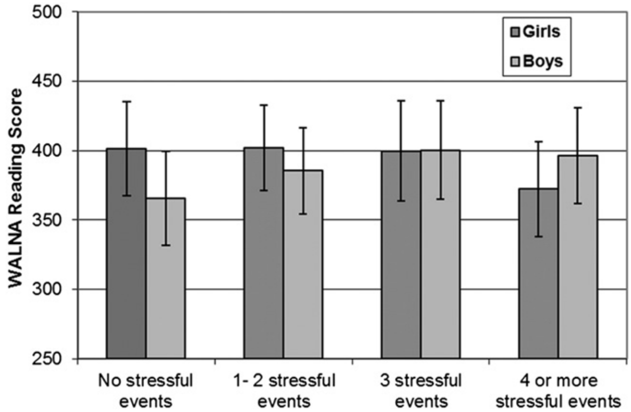


**Figure.** Maternal exposure to stressful life events in pregnancy and reading score at age 10 years.

stress events (372). However, in boys, the score began to increase by approximately 20 points, from 366 to 386, with 1-2 stress events, and increased further to 400 points with 3 events, before decreasing somewhat to approximately 396 points with maternal exposure to 4 or more life stress events.

Boys whose mothers experienced life stress events at any time up to 34 weeks' gestation had a higher average reading score by approximately 33 points compared with no stress exposure (Table III). The timing of the exposure had no significant effect on girls' reading scores.

Girls whose mothers experienced the death of a friend or a relative during pregnancy had lower mean reading scores, by 97 and 35 points, respectively. However, in boys, maternal exposure to pregnancy and money problems was associated with higher mean reading scores, by 21 and 27 points, respectively.

### Spelling, Writing, and Mathematics

Further multivariate analyses (not shown) with adjustment for the potential confounders showed that neither the timing nor the type of life stress events during pregnancy was associated with spelling, writing, or mathematics in girls. In boys, maternal exposure to 3 life stress events during pregnancy was associated with an increase of 36 points (95% CI, 4.32-67.40; $P = .03$), and exposure to 4 or more life stress events was associated with a 42-point increase (95% CI, 10.19-72.19; $P = .01$) in numeracy score, and exposure to residential move was associated with a 42-point higher mean writing score (95% CI, −11.97 to 72.74; $P < .02$).

## Discussion

Maternal exposure to 4 or more stressful life events during pregnancy was associated with lower reading scores in their female offspring at age 10 years. Specifically, the death of a relative and/or the death of a friend in pregnancy was linked to lower reading achievement in girls, independent of maternal sociodemographic characteristics, family income, maternal smoking during pregnancy, and common life stress events in infancy and middle childhood. No specific timing of antenatal exposure to life stress events was linked to school achievement in either girls or boys at age 10 years. When antenatal exposure to life stress events was analyzed as a single weighted scale, the overall findings remained largely unchanged, with one caveat: The negative effect of life stress events during pregnancy on reading decreased somewhat, suggesting that the effect may be attributed in part to life stress events at age 1 year, also a critical period for brain development.[33]

Overall, our findings in girls corroborate limited previous research that has linked maternal stress during pregnancy to offspring's reduced achievement in reading and mathematics at age 6 years (grade 1).[20] However, in contrast to Niederhofer and Reiter's study, which was based on teacher-reported academic marks at age 6 years,[20] our measures of academic achievement were derived from the scores on a standard statewide test administered at age 10 years.

Van den Bergh et al[34] proposed a fetal programming hypothesis in which a mother's exposure to stress or anxiety in pregnancy raises her levels of cortisol, which in turn crosses the placenta to affect the fetus and disturb ongoing fetal growth and development.[35] This hypothesis implies that maternal antenatal stress can affect fetal brain development, including the stress-regulatory hypothalamic-pituitary-adrenal axis, limbic system, and prefrontal cortex. Disruption of fetal brain development by maternal stress could have long-term consequences for cognitive development after birth. Whether excess glucocorticoid exposure is the only biological mechanism that links maternal stress in pregnancy to offspring's cognitive and academic performance is unclear. Vascular compromise of the placenta and undernutrition of the developing fetus due to maternal stress exposure are also known to shape fetal programming. However, these biological events seem to be associated more with systemic disease development during the course of life.[35] To better understand the biology underpinning developmental programming, future studies will need to collect information about such biological indicators in pregnant mothers exposed to life stress events.

One of the most consistent findings of previous studies on maternal stress in pregnancy and neurobehavioral development is an increased risk for attention deficit hyperactivity disorder in children.[7] Research also has linked maternal prenatal psychosocial stress to poor working memory in female offspring in young adulthood.[34,36] It is plausible that maternal antenatal exposure to life stress events leads to poor attention span in children, which in turn may negatively affect reading comprehension. However, this does not explain our discordant findings in boys versus girls in the present study.

In contrast to the negative effect of maternal exposure to multiple life stress events during pregnancy on reading achievement in the girls of our study population, boys whose mothers experienced 3 or more life stress events during pregnancy or reported pregnancy or money problems had significantly higher reading scores. When measured as a weighted scale, antenatal stress exposure also had a significant positive effect on reading in boys. Van den Bergh et al[34] reported that high antenatal maternal anxiety was associated with impulsivity during performance of cognitive tasks in 14 to 15-year-old adolescents, with boys more susceptible to this influence than girls. However, our results cannot be directly compared with that study, owing to differences in both outcome variables (performance of cognitive tasks in the previous study vs numeracy and literacy scores in the present study) and the measures of antenatal stress (subjective experiences of emotions/tension in the previous study vs exposure to life stress events during pregnancy in the present study).

Our finding of higher reading and writing scores in boys whose mothers experienced moderate stressful events during pregnancy is interesting in the context of the nonhuman literature. A range of studies conducted in laboratory animals has shown that prenatal stressors can cause feminization of neurobiological structures, hormones, and neurotransmitters in males, with corresponding effects on behavior.[37] In particular, even though maternal stress increases corticosteroid levels in both males and female fetuses, only in males does it decrease fetal testosterone and brain aromatase activity, and alters brain catecholamine activity to approach that in females. It is import to note, however, that in prenatally stressed females, the size of the anterior commissure was reduced to that in control males. It is also useful to note that some animal studies have shown a link between mild gestational stress and improved learning in male rats.[38,39] In humans, an inverse correlation between fetal testosterone concentration in utero and emerging language skills in toddlers has been reported.[40] Reading and writing are important measures of language skills, which are areas of cognitive strength in females.[41] The positive association between prenatal stress exposure and improved literacy skills in boys seen in our study population might be underpinned by a process similar to the feminization of neurobiological structures found in male animals.

In human research, DiPietro et al[42] reported a positive association between a low to moderate level of prenatal subclinical anxiety, stress, and depression and advanced motor and mental development at age 2 years. In another study, elevated levels of maternal cortisol late in gestation were associated with accelerated cognitive development over the first year and higher scores on the Bayley Scales of Infant Development at age 12 months.[3] Although DiPietro et al[42] tested for but did not find significant sex differences (possibly because of the small total sample size [n = 95]), and Davis and Sandman[3] did not test for sex differences, their findings show that a positive effect of moderate prenatal stress on offspring cognitive outcomes is possible.

We conducted 2 sets of 3-group and 11 sets of 2-group null hypothesis tests, and multiple testing could be an issue. Nonetheless, our findings clearly show that the direction of associations between maternal life stress events in pregnancy and reading achievement is negative for girls but predominantly positive for boys. The magnitude of the association is substantial, where with $P \leq .05$, for example, the decrease in reading score for girls was between 33 and 97 points, equivalent to 1/4 of the SD (104), whereas in boys the increase is between 22 and 42 points, or 1/5-2/5 of the SD. Furthermore, these sex differences remained unchanged when maternal life stress events in pregnancy was measured and analyzed as a single weighted scale, where multiple testing is not an issue. Thus, it is unlikely that the sex differences identified in this study are attributable to a chance effect. Our preliminary analyses based on pooled data showed no significant association between maternal exposure to life stress events and school achievement, because the effects in males and females "averaged out" when both sexes were combined. Thus, our findings highlight the importance of examining possible sex differences, and illustrate that failure to do so will lead to erroneous conclusions.

In contrast to most previous studies, the present study was based on a relatively large number of participants with longitudinal data obtained on exposures to life stress events during pregnancy and postnatally. In this study, we examined robust measures of literacy and numeracy as outcome variables, and we were able to adjust for a range of potential confounders. We examined different aspects rather than only a single dimension of maternal life stress events during pregnancy and identified significant sex differences in the effect of maternal exposure to life stress events on reading achievement in children, with important implications for future research. A limitation of this study is the lack of biological measures of maternal stress hormone levels during the life stress event exposures. We were unable to determine the extent to which self-reported life stress events were correlated with maternal cortisol levels; thus, the biological pathways linking maternal antenatal stress exposure to child developmental outcomes remain hypothetical.

Exposure to multiple stressful life events during pregnancy was negatively associated with reading scores in girls. The death of a relative and/or death of friend in pregnancy was particularly detrimental to the reading achievement of female offspring. Based on these findings, social support for mothers exposed to such life events during pregnancy may be recommended as an integral part of antenatal and postnatal care for mothers and children. Further research is needed to confirm our findings and explore biological and other pathways through which maternal exposure to life stress events during pregnancy affects male and female offspring differently. ■

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