

Meta-Analytic Findings of the Relation Between Maternal Prenatal Stress and Anxiety and Child Cognitive Outcome

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ABSTRACT: *Objective:* Different studies have revealed mixed findings regarding the relation between maternal prenatal stress or anxiety (MPSA) and early child cognitive outcome. Different methodological considerations may be linked to the absence of clear support for this hypothesized link. The purpose of this article was to conduct a meta-analysis of this relation while considering the following as potential moderators: (1) pregnancy trimester during which MPSA was assessed, (2) type of MPSA assessment (life events, pregnancy related, subjective assessments), and (3) research design (retrospective or prospective). Other moderators were also examined: child age at assessment and the year of publication. *Method:* Eleven studies were identified (N = 5903) that examined the relation between MPSA and early child cognitive outcome. *Results:* A small effect size of $r = -.05$ was found for this relation. The effect size varied across studies and was significantly moderated by the manner in which MPSA was operationalized (events, subjective assessment of stress or pregnancy-related stress or anxiety) and by whether MPSA assessment took place before or after infant birth. Greater relations to child cognitive outcome were found for postnatal event-based indicators of MPSA. *Conclusion:* The relation between MPSA and child cognitive outcome seems to be present, but low. Moreover, it is affected by the specific choices made by researchers in the manner in which constructs are operationalized.

(*J Dev Behav Pediatr* 0:1–6, 2013) **Index terms:** prenatal stress, child cognitive development, meta-analysis.

There has been increasing scholarly interest in maternal prenatal stress or anxiety (MPSA) as a fetal programming component of early child cognitive developmental outcome.^{1,2} Much of this interest was first generated in highly controlled experiments with rodents and primates, involving randomized trials and manipulations of levels of MPSA. These studies have convincingly shown that MPSA adversely influences different aspects of the offspring's cognitive functioning and learning.^{3,4} Studies with humans, which cannot benefit from randomized trials in the same way, also showed that MPSA is linked to different measures of infant and early childhood cognitive development. For example, Keim et al² followed 358 expecting women

during their pregnancy and showed that self-reports of stress and anxiety were related to infant language and cognitive development at the age of 12 months. King and Laplante examined the development of 150 infants whose mothers were exposed to the 1998 Quebec Ice Storm during their pregnancy. The Quebec Ice Storm was a natural disaster that caused massive power outages and forced many women to be out of their homes for several days, sometimes weeks. Objective indices of stress related to the ice storm were linked to both language and cognitive markers of development.⁵ A follow-up of 89 participants from this sample when children were 5½ years old, revealed that this association persisted.⁶ Finally, Gutteling et al⁷ showed that self-reports of MPSA predicted an index of concentration and attention when children were aged between 6 and 7 years. Other researchers have obtained similar findings and have contributed to the growing consensus around the notion that there is a relation between MPSA and early child cognitive development.^{1,8–10}

This growing consensus, however, masks some of the inconsistencies in results. Not all studies have supported the MPSA-child cognitive development link; and among those that have, not all reported measures of stress and anxiety are related to cognitive outcome.^{7,9} Sometimes results reveal a counter-intuitive relation between MPSA and cognitive outcome.^{2,8} Moreover, when significant effects are found, effect sizes range considerably. The

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purpose of this report is to conduct a meta-analysis of studies that have addressed the relation between MPSA and early child cognitive development by considering all reported associations between the 2 sets of variables across studies and to examine the potential contribution of different moderators in understanding this association.

Moderating Factors

At least 3 reasons might account for the between-study variability in effect sizes in studies that have addressed the MPSA-child cognitive outcome relation: First, several researchers have suggested that the time at which stress is measured during pregnancy may explain the differential variations in child cognitive outcome.^{8,11,12} Different studies suggest that rapid fetal growth, and particularly rapid cerebral growth, makes the fetus more vulnerable to organizational influences such as the maternal hormones that may cross the placental barrier in high concentrations during periods of stress.⁴ In this regard, Weinstock⁴ has suggested that late second and third trimester stress may have the greatest influence on learning, attention, and other factors that are critical for early postnatal development. However, empirical results have been mixed. For example, King and Laplante found that moderate-to-high exposure to stress in the first and second trimesters yielded greater deficits in infant cognitive development. The same authors found no trimester effects for language development.⁵ Davis and Sandman conducted a careful, prospective longitudinal investigation where repeated measures of maternal prenatal cortisol and self-reports of stress were obtained and infants were followed up until the age of 12 months. Their results indicated that elevated rates of maternal cortisol early during pregnancy were associated with lower cognitive performance in infants during the first year, whereas elevated rates later during gestation were associated with accelerated cognitive development.⁸ However, in contrast to King and Laplante, this study did not include MPSA assessments of the first trimester. Moreover, some researchers have obtained null findings for several measures of stress and child cognitive outcome, whereas others have found later stress to be inversely associated with cognitive development in early childhood.⁹ Although there are hypothetical, physiological explanations that may account for time of stress during pregnancy as a moderator of the MPSA-child cognitive development link, the empirical data seem to be inconclusive in this regard and merit closer attention.

A second factor that might account for some of the inconsistencies in results that have been observed is the variety of measures that have defined the maternal stress or anxiety concept. Some researchers have relied on maternal self-reports of different stress or anxiety related constructs.² Whereas, others have relied on the objective occurrence of major life events. King and Laplante had mothers report on the objective events that they had to cope with in the aftermath of the Quebec Ice Storm, and

their subjective experience of stress regarding these events. Here, it was found that reference to objective events, rather than subjective assessments of stress, related to child cognitive outcome.^{5,6} Other researchers report on more than 1 measure with different levels of association documented with cognitive development for each measure.^{1,2,7} As with much of stress research, the concept is defined and operationalized in different ways; and it is reasonable to expect that links with child cognitive development may vary on this basis. We will investigate whether systematic differences in effect size in the MPSA-child cognitive outcome link might be attributable to the manner in which stress is operationalized.

A final moderator that may explain variation in the distribution of effect sizes is the prospective or retrospective nature of the research design. Researchers have typically asked expecting mothers to provide MPSA data during their pregnancy, however, in some cases MPSA data are procured weeks or months after the birth of the child. In the case of King and Laplante, the objective events that are at the core of the stress assessment take place during the mother's pregnancy, but the assessments of these events take place at least 6 months after the infant's birth.⁵ Bergman et al¹³ assess prenatal stress more than a year after the birth of the infant. Although authors go to different lengths to control for possible biases that retrospective assessments of stress may entail, it remains possible that different factors may influence postnatal assessments of prenatal stress and provide systematic differences in the effect sizes that are observed.

The purpose of this meta-analysis was to test the overall effect size of the relation between MPSA and child cognitive development, as well as the roles of the time of assessment, type of MPSA assessment, and whether the research design was prospective (prenatal assessments of MPSA) or retrospective (postnatal assessment of MPSA). In addition, child age and the year of publication are also considered. The latter are often considered as potential study-based moderators of effect size.

METHOD

Study Selection

The selection of pertinent articles was based on the following 3 steps. First, articles were initially selected using the medical and psychological search engines MEDLINE and PsycINFO for the period between 1970 and 2011 with the following key words: maternal stress, prenatal stress, foetal programming, infant development, intelligence, WPPSI, prenatal anxiety, stress pregnancy, Bayley, BSID, infant development, child development, cognitive development. Each key word was used alone and in combination with the others.

Inclusion and Exclusion Criteria

Studies had to include an assessment of maternal prenatal stress or anxiety (MPSA) and an assessment of

child cognitive development when children were aged between 0 and 60 months. When the same sample was reported in more than 1 study, the most exhaustive reporting of the sample was maintained for analysis and the others were excluded.

A total of 17,066 articles were identified in this first step. After reading study titles and abstracts, we retained 30 studies. Further reading of each article led to our retaining 20 articles. The second step involved a search of the reference lists of these 20 articles, which yielded an additional 3 references. Finally, 11 authors considered to be specialists in this area were contacted and asked for references. In total, they supplied 196 references, all of which had been part of previously examined lists of articles.

Of the 23 articles identified, 12 were eliminated because they provided data on samples presented more exhaustively in other articles. Thus, a total of 11 studies, reporting 27 MPSA-child cognitive outcome effect sizes were identified as relevant for this study. These studies include a total N of 5903 mother-child dyads. Sample size ranges from 66 to 3139. Table 1 presents the studies used in analyses.

Coding of studies

Studies meeting inclusion criteria were coded by 2 coders as a function of 4 characteristics:

1. Gestational trimester covered by the assessment of MPSA. Some studies provided a general prenatal score covering the gestational period, some at a single time during the prenatal period and others reported more than 1 assessment of MPSA during gestation.^{8,14,15}

2. Operationalization of MPSA. We distinguished between 3 kinds of assessments that were present in the literature: (1) objective indices of stress—these included counts of major life events or exposure to catastrophic and associated events⁵; (2) stress and anxiety related to the pregnancy, childbirth or the health of the infant⁸; and (3) other subjective, cognitive appraisals of stress or anxiety.^{5,9}
3. Research design. Here, studies were divided into 2 groups: those that assessed MPSA before infant birth and those that addressed MPSA after infant birth.
4. Finally, we coded for 2 study characteristics that were perceived as potential effect-size moderators: child age at assessment and the year of publication.

Coders reached perfect agreement as to each of the 4 coding criteria.

Meta-Analytic Procedures

The meta-analysis was conducted using Comprehensive Meta-Analysis Version 2.0.¹⁶ A measure for effect size (Pearson *r*) was calculated for each study. When a study provided results for different independent or dependent variables, it was because different indices of stress or anxiety were reported in relation to cognitive development. Average effect sizes for each study were used to test for the overall relation between stress and cognitive development. However when considering moderating effects, each effect size was used independently to ensure that different kinds of indices of stress or anxiety were appropriately considered. Combined effect sizes were calculated and tests for various moderators conducted using a random-effects approach.¹⁷

Table 1. Studies Included in Analyses

Authors	N	Trimester ^a	Stress Evaluation	Time of MPSA Assessment	Cognitive Development Assessment
Bergman et al ¹³	123		Life events	Postnatal	BSID
Brouwers et al ²⁴	105	3rd	Subjective assessment	Prenatal	BSID
Davis and Sandman ⁸	125	2nd and 3rd	Subjective assessment, pregnancy-related	Prenatal	BSID
DiPietro et al ²⁵	82	2nd and 3rd	Subjective assessment, pregnancy-related	Prenatal	BSID
Grant et al ¹⁵	105	3rd	Subjective assessment	Prenatal	BSID
Henrichs et al ²⁶	3139	2nd	Subjective assessment	Prenatal	MacArthur
Huizink et al ⁹	170	2nd and 3rd	Subjective assessment, pregnancy-related	Prenatal	BSID
King and Laplante ⁵	150		Life events, subjective assessment	Postnatal	BSID, MacArthur, WPPSI
Lou et al ¹⁰	120	2nd	Life events	Prenatal	Prechtl
Slykerman et al ¹⁴	1714		Subjective assessment	Postnatal	Stanford-Binet
Van den Bergh ²⁷	70		Subjective assessment	Prenatal	BSID, Prechtl

^aWhen trimester data are not reported, it is either because studies are retrospective, measures were taken at different times during pregnancy, or treatment of data prevented inclusion of this variable in this analysis.

RESULTS

Results are presented in Table 2. Globally, there seems to be a low but significant inverse association between indices of maternal prenatal stress or anxiety (MPSA) and early child cognitive development ($k = 11$; $r = -.05$; $p < .0001$; 95% confidence interval [CI], $-.07$ to $-.02$). Significant heterogeneity of results across studies is noted however ($Q = 47.43$; $p < .0001$), making it pertinent to investigate potential moderating variables.

The available data allowed for 17 effect sizes to be analyzed as a function of the trimester of pregnancy when MPSA assessments were made: 1 in the first trimester, 8 in the second trimester, and 8 in the third trimester. No differences in the effect size were noted as a function of the trimester during which MPSA was measured. This was the case whether the first trimester study was excluded or included in the group with second trimester data.

Twenty-seven effect sizes are reported across the 11 studies for the different categories of MPSA assessments: life event-based assessments, pregnancy-related measures, and subjective measures of stress or anxiety. Although all effect sizes are in the same direction, the effect size for the relation between life-events and cognitive development ($k = 4$; $r = -.31$; $p < .0001$; 95% CI, $-.40$ to $-.22$) is significantly greater (both $p < .001$) than that for pregnancy-related stress or anxiety ($k = 7$; $r = -.08$; 95% CI, $-.14$ to $-.02$) or other subjective assessments of stress or anxiety unrelated to pregnancy ($k = 16$; $r = -.02$; 95% CI, $-.05$ to $.01$).

Eight studies used prospective and 3 used retrospective assessments of MPSA. Both effect sizes are in the same direction; however, there is a significant difference between the 2 groups of associations. Retrospective, postnatal assessments yield significantly greater effect

sizes ($k = 3$; $r = -.11$; $p < .001$; 95% CI, $-.16$ to $-.06$) than prospective, prenatal assessments of MPSA ($k = 8$; $r = -.03$; $p < .001$; 95% CI, $-.06$ to $-.01$).

No systematic variation in the effect size was found as a function of child age when cognitive assessments were made or for the year in which the study was published.

DISCUSSION

The results of the present meta-analysis underline 2 critical points. First, there seems to be a consistent, low-level association between maternal prenatal stress or anxiety (MPSA) and later child cognitive development. Even in the low-risk circumstances that most pregnancies afford in the western world, where almost all of the current studies were conducted, stress and anxiety during pregnancy are meaningfully and negatively associated with later child cognitive outcome. The magnitude of the effect size is similar to that obtained when examining the relation between MPSA and birth-related variables such as Apgar scores, birth weight, or gestational age and supports the current consensus surrounding the proposal that maternal stress and anxiety are related to fetal programming processes beyond the immediate perinatal circumstances, even under normative, low-risk circumstances.¹⁸

However, results do vary significantly across studies, indicating that potential moderating variables are worth considering and that further study in this area be conducted with care. Specifically, the results reveal that studies that report on more objective life events as indicators of MPSA yield greater effect sizes than those that pertain to pregnancy-related stress or other subjective indicators of the MPSA experience. Although the number of effect sizes reported for each of the definitions of MPSA is low and thus should be considered as

Table 2. Association Between Maternal Prenatal Stress or Anxiety and Child Cognitive Development for All Reported Effect Sizes and as a Function of Moderators

Moderator	<i>k</i>	<i>N</i>	<i>r</i>	95%		Homogeneity <i>Q</i>	Slope
				CI Inf	Sup		
All studies	11	5903	-.05***	-.07	-.02	47.43***	
Trimester							
1st and 2nd	9	3636	-.02	-.05	.01	36.67***	
3rd	8	587	-.09**	-.15	.02	14.08*	
MPSA assessment							
Life events	4	393	-.31***	-.40	-.22	7.17	
Subjective assessments	16	5660	-.02	-.05	.01	29.05*	
Pregnancy-related	7	377	-.08**	-.14	.02	11.02	
Research design							
Prospective	8	3916	-.03*	-.06	-.01	26.01**	
Retrospective	3	1987	-.11***	-.16	-.06	14.09**	
Publication year	11						.01
Child age	11						.00

* $p < .05$, ** $p < .01$, *** $p < .001$. CI, confidence interval; Inf, inferior; MPSA, maternal prenatal stress or anxiety; Sup, superior.

preliminary and in need of replication, the differences seem substantial and suggest that further thought be given to the manner in which MPSA is operationalized across studies. Almost all effect sizes reported, including those involving other moderators, hover fairly close to the global effect size of $-.05$, with the exception of studies where major events are used as an indicator of stress, where $r = -.31$. Such a finding suggests that the events that mothers experience during their pregnancies, perhaps more than their cognitive appraisals of those experiences themselves, may hold a closer relation to ongoing biological processes involved in fetal cerebral growth. The relation between life events and child cognitive outcome may be suggestive of other developmental processes that are not addressed in this meta-analysis. For example, several studies have shown that the frequency of stressful life events is associated with more general socioeconomic factors, where people living in otherwise more vulnerable circumstances experience greater challenges in their everyday lives, including greater numbers of events that require adaptation. It is certainly conceivable that expecting women from more difficult circumstances may also be experiencing more frequent events that draw on their adaptive resources. It is possible that a relation between life events and early childhood cognitive development may well reflect ongoing mediation processes linking socioeconomic strain and child developmental outcome. In such a scenario, fetal programming is part of a social selection process, where socioeconomic risk actually precedes pregnancy, which serves to mediate risk.¹⁹ Further study will require close monitoring of such socioeconomic factors and their relation to life events and child outcome.

The relation between MPSA and child cognitive development was also moderated by the study design. Studies in which MPSA assessments were conducted after the birth of the child yielded significantly greater effect sizes. At least 2 possible interpretations of this finding can be made. First, as with other studies in cognition and memory, this finding suggests that studies where retrospective assessments of MPSA are made should be viewed with some caution. Retrospective reports have certain clear advantages in helping researchers identify more clearly mothers who are at greater risk for MPSA and some of the findings from such studies may well reflect underlying processes that are difficult to parse out in prospective studies. But, it is also possible that postnatal assessments of MPSA may inflate relations between the 2 constructs. Postnatal assessments are methodologically closer in time to outcome assessments, and they may be subject to memory biases that are difficult to control and which may inflate effect sizes.²⁰ Conversely, it is possible that pregnancy imposes certain cognitive interpretations of events and circumstances such that, perhaps, postnatal assessments may yet be accurate indicators of MPSA and contribute to our understanding of its link to child outcome. We have labeled this possibility the “keep the course” hypothesis.

Here, expecting mothers may well use cognitive coping skills that help them modify appraisals of stress for adaptive needs in the prenatal period but are free to more objectively appraise MPSA in the postnatal period. For example, if an expectant mother experiences stressful circumstances during the period preceding birth, to preserve the pregnancy process, she may reduce the importance of this situation if asked about it prenatally, but more objectively assess it in the weeks and months after the birth of the infant, especially if some resolution of the issue is under way. A careful analysis of the relation between prenatal and postnatal MPSA assessments has yet to be studied in any meaningful way that might inform both possibilities.

This meta-analysis is limited on at least 4 levels. First, only 11 studies were involved, reporting 27 different effect sizes. More studies, including different samples, from different populations, are required to increase confidence in the meta-analytic estimates that presently emerge. The absolute number of samples that might inform researchers regarding this association needs to be increased significantly.

Second, in only 2 samples was there a meaningful attempt to account for postnatal processes that may be involved in cognitive development.^{5,13} Such processes have been found to be related to language and cognitive development and require greater scholarly attention when attempting to parse out the influence of MPSA on outcome.²¹ These processes include mother-infant and father-infant interactions and the establishment of the early attachment relationship and the general quality of family relations and the home environment. Such processes may serve to mediate the MPSA-cognitive development link, in that stress and anxiety in parents may be associated to lower quality parent-child interactions after the birth of the child.²² These processes may also serve a moderating function, as Bergman et al¹ have suggested. These authors found that the postnatal processes related to attachment security seemed to attenuate any prenatal stress effects on infant development. Both prenatal and postnatal processes have been called on to account for different aspects of development and a clearer understanding of the relative contributions of both classes of variables will emerge as researchers simultaneously consider them in their research designs.

Third, the reviewed studies did not account for possible covariates of MPSA, most notably those that might be linked to depression and other mood disorders and their symptoms. There has been considerable interest in addressing the association between such prenatal aspects of adjustment and infant and child developmental outcome. To gain better insight into the specific contribution of MPSA to cognitive development, it will be helpful to partial out variance that might be attributable to other aspects of prenatal adjustment that may be involved in fetal developmental processes.²³

Finally, almost all measures of cognitive outcome are general assessments, with an emphasis on the Bayley

Scales of Infant Development, perhaps to be expected given the age range that was investigated. It will be helpful in future research to use more specific indicators of cognitive outcome related to information processing, memory, language development, or other aspects of cognitive functioning to more accurately draw out the relation between MPSA and cognitive development.

The 17 effect sizes that included pregnancy trimester when stress measures were taken yielded no significant differences between second and third trimester assessments. Although such preliminary data speak to the issue of the time during which MPSA is assessed, it is possible that different factors contributed to the absence of significant findings for this moderator, namely the quasi absence of first trimester assessments and the very general nature of some assessments, which did not assess the timing of MPSA experiences per se, but rather reflected the time when assessments were conducted. Still, finely grained studies reveal such differences and others have provided physiological theory that might account for such effects and, as such, the current null findings indicate the need for greater detail to be brought to studies that address this methodologically complex issue.⁸

Although these meta-analytic results confirm current consensus regarding the relation of MPSA to early infant and child cognitive development, the suggestion is made that this association is relatively low throughout the 11 studies that were examined and moderated by specific study characteristics, namely the manner in which MPSA is assessed and whether measures are made prospectively, before infant birth, or retrospectively, after the child is born. Furthermore, detailed study is called for that focuses on the processes by which these and other moderators may operate.

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