

Original Article

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Maternal pre-pregnancy weight and twins' temperament

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Abstract

Maternal pre-pregnancy weight has been related with young singletons' cognitive and behavioral development, but it is not clear if it has an effect on temperament. We used a twin cohort to evaluate the association between maternal pre-pregnancy body mass index (BMI) and infants' temperament. The mothers of 834 twins answered questions regarding their pre-pregnancy BMI and their 0- to 18-month-old children's temperament using the Revised Infant Behavior Questionnaire. Three temperamental dimensions were examined: activity level, distress to limitation and duration of orienting. The relationship between maternal pre-pregnancy BMI and each temperamental component was investigated by means of multilevel mixed-effects linear regression analysis. We found no clear evidence of an association of maternal pre-pregnancy BMI with twins' temperament. The development of temperament is influenced by a large number of factors, probably different from those influencing children's emotional and behavioral development.

Introduction

Temperament refers to individual differences in emotional, motor and attentional reactivity measured by latency, intensity and recovery of response, and self-regulation processes such as effortful control. Rothbart and Derryberry¹ suggested that infant temperament can be assessed by the degree to which infants react and regulate their responses. Since reactivity is the response to external stimuli and regulation is the manner in which the infant returns to homeostasis, differences in individual infant reactions can be assessed behaviorally and understood biologically.

An increasing body of literature has suggested a link between temperamental aspects and child psychopathology.^{2,3} Specifically, three dimensions of the broad temperamental components have been linked with the development of psychopathology later in life^{4–6}: *activity level* (gross motor activity, including squirming and locomotor activity), *distress to limitations* (fussing, crying or showing distress when confined in a place/position or when unable to perform a desired action) and *duration of orienting* (attention to and/or interaction with an object). Infants high in distress are at greater risk of being more aggressive.⁷ A meta-analysis on the relationship between problems in infancy and long-term behavioral outcomes suggests that high distress, usually manifested as excessive crying, in the first year of life is predictive of attention problems at school age.⁸ Persistent problems with behavioral control, such as the inability to regulate feeding and sleeping behavior in infancy, are precursors of behavior control difficulties such as hyperactivity or conduct problems in childhood.^{9–11} Finally, difficulties with anger regulation are associated with attention problems from preschool through adulthood.^{12,13}

Previous research has examined the genetic and environmental etiological factors of infant temperament development.^{14–16} Twin studies provide strong evidence of genetic influence on temperament including activity,¹⁷ distress¹⁶ and attention.^{18,19} Estimates of heritability suggest that genetic factors account for 20–60% of the variability of temperament within a population with no consistent pattern of differential heritability across dimensions.²⁰

The influence of prenatal environment on children's temperament and behavior is probably less strong than the influence genetic factors have.²¹ In general, a genetically informative study design helps controlling for a large number of confounders that might affect the results. However, the prenatal environment experienced by twins may be different from the one

singletons experience. This is mainly due to space and nutrients scarcity, which could lead to various growth complications.²² Moreover, it is possible that monozygotic (MZ) twins, as compared to singletons and dizygotic (DZ) twins, face a more challenging environment while in the uterus, as a very large proportion of them share one chorion.²³ However, no study has reported a significant influence of chorionicity on temperament,²³ while an older study²⁴ showed that there is no clear pattern of genetic influences in the neonatal period and no significant differences between the MZ and DZ twins correlations, suggesting the presence of shared prenatal environmental influence on temperament.

Since both pregnancy and obesity are associated with massive metabolic alterations acting together, they might impact the environment experienced by the fetus. It has been hypothesized that maternal adiposity at the time of conception may be important for child mental health programming, since the prenatal development of the brain might depend on the level of maternal energy supply.^{25,26} However, the possible influence of maternal weight before pregnancy, as a proxy for the prenatal environment, on children psychological development has only recently been studied. Van Lieshout *et al.*²⁷ analyzed the association of maternal pre-pregnancy body mass index (BMI) with offspring temperament and behavior in children aged 1 year and 2 years, respectively. In their analysis, maternal BMI was not found to be related with any temperamental component, measured using the Toddler Temperament Scale, nor with internalizing behavior. However, a higher maternal BMI was found to be positively associated with elevated externalizing problems at age 2.²⁷ Higher maternal pre-pregnancy BMI was also predictive of a high degree of distress and inattention^{28–30} and a tendency for child aggressive behavior.³¹

To the best of our knowledge, there are no studies on the relationship between maternal pre-pregnancy weight and twins' temperament. In the present study, we used maternal pre-pregnancy BMI as a proxy of the shared prenatal environment to evaluate its influence on infants' temperament in MZ and DZ twins. A deeper understanding of this association could help preventing the development of difficult temperament in children, as well as antisocial behavior later in life, by informing prospective mothers on the possible effects of overweight and obesity on children's psychopathology.

Method

Study population

The Twins and Multiple Births Association Heritability Study (TAMBAHS) is a volunteer-based study focusing on the development of twins from birth until 5 years of age. For the present study, mothers of twins aged 0–18 months at the time of the survey were identified. Between July 2008 and May 2010, 417 mothers completed the study's self-assessed questionnaire on their twins' temperament. For the determination of the twins' zygosity, the adapted version of Goldsmith's zygosity questionnaire was used.³² This adapted questionnaire, as a method of assigning zygosity, has been validated against determination by identity of polymorphic DNA markers and has reached accuracy in verifying zygosity in 95% of cases.³³ In total, 834 twins were included in the analyses; 188 MZ male twins, 188 MZ female twins, 120 DZ male twins, 118 DZ female twins and 220 opposite-sex twins.

Maternal and twins' characteristics

Pre-pregnancy BMI (expressed as kg/m²) was based on maternal self-report of weight and height and introduced as a continuous variable in the linear regression analysis. Gestational age (measured in completed weeks of gestation), level of education (high school diploma or less, college/professional education and university degree), employment status (housekeeper or unemployed, working part-time, working full-time and others) and smoking (before, during, after pregnancy; yes/no) were noted for mothers; age (in months), sex and birthweight (in grams) were noted for all twins.

Temperament

Infant temperament was assessed using the revised Infant Behavior Questionnaire (IBQ-R).³⁴ The parents were asked to report on a seven-point Likert-type scale the relative frequency of occurrence of specified infant reactions to concrete situations during the previous 7 days. The scale ranged from 1 to 7 (never, very rarely, less than half the times, about half the times, more than half the times, almost always, always and does not apply). The IBQ-R consists of 14 scales. For the purposes of this study, we used only three dimensions of temperament: (1) activity level, which consists of items examining the twins' movement of arms and legs, squirming and locomotor activity; (2) distress to limitations, which consists of items looking into twins' fussing, crying or showing distress while (a) in a confining place or position; (b) involved in caretaking activities; (c) unable to perform a desired action; (3) duration of orienting, which consists of items on the twins' attention to and/or interaction with a single object for extended periods of time. Reliability, convergent validity and relative stability have been demonstrated for the IBQ-R.^{35,36} The internal consistency for the IBQ-R items was high with the Cronbach's α , ranging from 0.81 to 0.90. Consistency between parent report on the IBQ-R and indicators of temperament based on home and laboratory observations has been demonstrated.³⁷

Statistical analysis

Mean and standard deviation (s.d.) or median and interquartile range for each continuous variable were calculated as appropriate, stratified by zygosity group. Intrapair twin correlations for each variable, subdivided into MZ and DZ twins, were calculated by using Pearson's (r) and Spearman's ^{ρ} coefficient statistics where appropriate.

The association between maternal pre-pregnancy BMI and each temperamental dimension was analyzed using a multilevel mixed-methods linear regression, in which a random-effect model was added to the default fixed-effects. The intercept of each twin pair was modeled as a function of the population intercept plus a unique contribution of the twin pair, as thoroughly explained by Carlin *et al.*³⁸ and summarized by the following equation:

$$Y_{ij} = \beta_0 + \beta_C X_{i(j)} + \alpha_i + \epsilon_{ij}$$

in which Y_{ij} represents the outcome (i.e., the specific temperamental dimension's score) of the j th twin in the i th pair. In addition to the linear regression model, a pair-specific error term (α_i) allows a random shift of the intercept. Regression coefficients (β_s) were used as a measure of change on the temperamental dimensions' scores by a unit change in the mother's BMI.

Table 1. Means/frequencies, standard deviations/percentages and Pearson correlations with the three temperament scales for each covariate, stratified by zygosity

Maternal characteristics	MZ twins					DZ twins				
	Mean or median	SD or IQR	r_a	r_b	r_c	Mean or median	SD or IQR	r_a	r_b	r_c
Pre-pregnancy BMI §	23.40	4.56	-0.04	-0.01	0.04	23.46	5.40	-0.03	-0.13*	0.00
Age (years)	33.47	4.22	-0.12*	-0.05	-0.10	34.65	4.05	-0.19**	-0.14***	-0.09
Gestational age (weeks) §	36	2.93	0.04	-0.06	0.06	37	3.71	0.03	0.03	-0.04
Smoking (yes)	<i>N</i>	%	r_a	r_b	r_c	<i>N</i>	%	r_a	r_b	r_c
Before	28	16	-0.03	-0.02	0.03	35	16	-0.03	0.09	0.04
During	4	2	0.00	0.07	0.03	11	5	0.02	0.07	-0.02
After	11	6	-0.04	0.02	0.16***	17	8	-0.03	0.09	0.9***
Level of education	<i>N</i>	%	r_a	r_b	r_c	<i>N</i>	%	r_a	r_b	r_c
High school diploma or less	33	18.6				47	21.1			
College/professional education	31	17.4	-0.15	-0.11	-0.07	52	23.3	-0.06	-0.13	-0.05
University education	114	64.0				124	55.6			
Employment status	<i>N</i>	%	r_a	r_b	r_c	<i>N</i>	%	r_a	r_b	r_c
Housekeeper or unemployed	192	53.6				216	47.8			
Working part-time	80	22.3	0.01	-0.19**	0.02	136	30.1	-0.04	0.04	-0.04
Working full-time	68	19.0				88	19.5			
Other	18	5.1				12	2.6			
Twin characteristics										
Birthweight (in grams) §	2438.06	793.78	0.08	-0.03	0.05	2590	708.74	-0.03	-0.03	-0.02
Age (months) §	8	8	0.35**	0.11*	0.10*	9	8	0.16**	0.04	0.20**
Sex	<i>N</i>	%	r_a	r_b	r_c	<i>N</i>	%	r_a	r_b	r_c
Male	188	50.00				120	26.20			
Female	188	50.00	-0.14**	-0.16**	-0.04	118	25.77	-0.03	-0.11*	0.07
Opposite sex	-	-				220	48.03			

§ Median (IQR) shown.

r_a Pearson/Spearman correlation with activity level.

r_b Pearson/Spearman correlation with distress to limitations.

r_c Pearson/Spearman correlation with duration of orienting.

* $P < 0.05$; ** $P < 0.001$; *** $P < 0.0001$.

Twins' age, gender, birthweight and gestational age, and maternal age, smoking (before, during and after pregnancy), level of education and employment status were adjusted for in the analysis.

All analyses were performed using STATA v.14.³⁹

Results

Descriptive statistics as well as Pearson and Spearman correlations between each covariate and the three temperament dimensions stratified by zygosity are shown in Table 1. Mothers' age was 33.47 years (4.22) for mothers of MZ and 34.65 years (4.05) for mothers of DZ twins. Mothers' BMI mean score was

23.40 (4.56) for mothers of MZ and 23.46 (5.40) for mothers of DZ, respectively. For MZ and DZ twins, respectively, the median [interquartile range (IQR)] for gestational age was 36 weeks (2.93) and 37 weeks (3.71); for birthweight it was 2438.06 g (793.78) and 2590 g (708.74). MZ and DZ twins were significantly different with respect to gestational age ($P = 0.0001$), birthweight ($P < 0.0001$) and maternal age ($P = 0.0001$).

Means of temperamental dimensions and intrapair twin correlations for MZ and DZ twins are shown in Table 2. For activity level, MZ correlation was $r = 0.75$ and the DZ correlation was $r = 0.45$. For distress to limitations, MZ and DZ correlations were $r = 0.83$ and $r = 0.56$, respectively. For duration of orienting, MZ and DZ correlations were $r = 0.94$ and $r = 0.85$, respectively.

Table 2. Descriptive statistics of temperament scales for monozygotic and dizygotic twin pairs

Temperament scales	Monozygotic twin pairs (n = 188)							Dizygotic twin pairs (n = 229)						
	Twin 1			Twin 2			<i>r</i>	Twin 1			Twin 2			<i>r</i>
	<i>N</i>	<i>M</i>	<i>s.d.</i>	<i>N</i>	<i>M</i>	<i>s.d.</i>		<i>N</i>	<i>M</i>	<i>s.d.</i>	<i>N</i>	<i>M</i>	<i>s.d.</i>	
Activity level	185	4.12	1.01	185	4.00	0.93	0.75**	215	4.13	0.98	215	3.99	0.95	0.45**
Distress to limitations	185	3.48	1.02	185	3.55	0.98	0.83**	215	3.57	0.99	215	3.58	0.97	0.56**
Duration of orienting	171	3.72	1.20	171	3.69	1.21	0.95**	202	3.57	1.13	202	3.53	1.18	0.85**

N: Number of twins; *M*: Mean; *r*: Within-twin correlations.

Twin 1 is the first born.

Twin 2 is the second born.

P* < 0.05; *P* < 0.001.

Linear regressions

Table 3 presents the results of the linear regressions. In the unadjusted analyses, we found a small decrease in the DZ twins' distress to limitations score for every unit increase of mother's pre-pregnancy BMI ($\beta = -0.03$; [95% confidence intervals (CI): $-0.050, -0.001$]; $P = 0.042$). This association was not substantially affected after important confounders were adjusted for ($\beta = -0.04$; [95% CI: $-0.065, -0.013$]; $P = 0.003$). Similar results were obtained when analyzing the MZ and DZ twins combined (results not shown). No association remained statistically significant after controlling for multiple testing: the statistically significance cut-off was set at $\alpha = (0.05/18) = 0.0028$. The normality of residuals was checked through normal quantile plots and confirmed for all regression analyses (results not shown).

Discussion

The aim of this study was to examine the relationship between maternal pre-pregnancy weight and infants' temperament, measured through three dimensions of the revised version of the IBQ: activity level, distress to limitation and duration of orienting. A statistically significant, negative association between maternal pre-pregnancy weight and distress to limitation in DZ twins initially emerged from the present analysis. However, the relative *P*-value failed to reach the critical level of significance after controlling for multiple testing. Although the Bonferroni method for multiple testing adjustment has been criticized and could be considered excessively conservative in this case,⁴⁰ the 95% CI clearly shows that the true value of β is close to null, falling between -0.065 and -0.013 . This means that for a 1-unit increase in maternal pre-pregnancy BMI, scores in distress to limitation would decrease on average by 0.04 points, on a 1–7-point scale. Consequently, the beneficial effect of a high maternal BMI on children's temperament we observed is certainly not enough to suggest that a higher maternal pre-pregnancy weight could be beneficial, especially in light of the many negative effects overweight and obesity have on perinatal outcomes and maternal and offspring's health.⁴¹

A large part of the literature suggests that the risk of cognitive and behavioral problems is associated with adverse intrauterine factors.^{29,30,42–45} Maternal pre-pregnancy overweight or obesity was associated with symptoms of attention-deficit/hyperactivity disorder (ADHD) in school-aged children³⁰ and in child with attention and behavioral problems.^{29,42} Furthermore, a UK-based,

longitudinal study analyzed the influence of maternal pre-pregnancy BMI on children's cognitive ability, reporting a statistically significant, negative association.⁴⁶ However, the effect size was as limited as the one reported in the present study, with a 10-point increase in maternal BMI being associated with a 1/10 s.d. decrease in cognitive performance at age 7 years. To the best of our knowledge, only one study has analyzed the possible influence of maternal pre-pregnancy BMI on singletons' temperament.²⁷ In spite of important methodological differences, such as the specific questionnaire used^{34,47,48} and the population of interest (i.e., singletons *v.* twins), there is consistency in the results between the present and Van Lieshout's study. Specifically, they reported that temperament at 1 year of age was not associated with maternal pre-pregnancy BMI. Of note, however, is that measures of externalizing behavior on the same population were found to be significantly associated with maternal pre-pregnancy weight. Another study, which analyzed children's behavior development and cognition in two separate, large cohorts in the United Kingdom and the Netherlands, found no consistent evidence of perinatal influence on these outcomes.⁴⁹ The strong association was observed with children's IQ at 8 years, while outcomes in younger children were not statistically significant after adjusting for critical confounders nor was repeated in both cohorts. Overall, most of the clinically significant results are reported in studies analyzing older children as opposed to infants and pre-school children, suggesting that the effect of maternal pre-pregnancy BMI may manifest later in children's development.

The biggest strength of the present study is that the population analyzed is a cohort of young twins. Analyzing twins instead of singletons, automatically controls for genetic (in MZ twins) and common environmental factors (in both MZ and DZ twins). It has been shown previously¹⁴ that temperament, as well as cognitive and behavioral development, has substantial genetic and environmental influences; therefore not having a genetically informed study design could be an important limitation of all the studies cited above, limiting the confidence in their significant results. Furthermore, the pre-pregnancy environment experienced by singletons may not be comparable with that experienced by twins. In fact, multiple pregnancies are often characterized by nutrient and space scarcity, which may lead to discordant growth or more serious, pathological complications, such as the twin-to-twin transfusion syndrome.²³ This implies that twins, and especially MZ twins, might be more susceptible to challenging intrauterine environment that might influence their future temperament. As far as we know, only one study explored the

Table 3. Linear regressions for the temperamental scales stratified by zygosity based on maternal BMI

		Monozygotic twins						Dizygotic twins					
		β coefficient	CI	<i>P</i>	β coefficient [^]	CI [^]	<i>P</i> [^]	β coefficient	CI	<i>P</i>	β coefficient [^]	CI [^]	<i>P</i> [^]
Outcomes by BMI													
Activity	Level	-0.01	-0.04, 0.02	0.57	-0.01	-0.04, 0.03	0.71	-0.01	-0.03, 0.02	0.61	-0.01	-0.04, 0.01	0.33
Distress to limitations		-0.00	-0.04, 0.03	0.94	0.00	-0.03, 0.04	0.88	-0.03	-0.05, -0.00	0.04 [§]	-0.04	-0.07, -0.01	0.003 [§]
Duration of orienting		0.01	-0.03, 0.06	0.61	0.02	-0.03, 0.07	0.37	0.00	-0.03, 0.04	0.98	0.02	-0.01, 0.06	0.25

SE: standard error of β .[^]Adjusted for twins' age, sex, mother's age, level of education, employment status and smoking (before, during and after pregnancy).[§] $P \leq 0.05$; * $P \leq 0.0028$.

association between maternal pre-pregnancy weight and twins' behavior,³¹ finding a tendency for children of overweight and obese mothers toward clinically aggressive and externalizing behaviors. It is therefore essential to analyze further the influence of perinatal factors on twins' psychopathological development.

A vast part of the literature focuses on children's cognitive and behavioral development as opposed to infants' temperament, limiting the comparability and understanding of the process. Various suggestions have been put forward for the explanation of the relation between temperament and psychopathology. Of the models suggested, one poses that temperament can be considered as a spectrum, or a common cause model, with normal and abnormal falling at different points on the same continuum. In essence, this model considers temperament to be a sub-clinical manifestation of psychopathology, with shared etiological determinants.⁵⁰ The results of the present study suggest, however, that some of the etiological factors important in emotional/behavioral problems, including maternal pre-pregnancy BMI, may not be important for specific temperamental dimensions. This suggests that temperament is not simply a manifestation of psychopathology with a shared etiology. Shiner and Caspi⁵⁰ have argued that it is implausible that complex behavior such as child psychopathology is the simple product of one or two temperamental factors. Instead, these temperamental factors likely interact with each other and with other variables such that the "true" impact of temperament is larger than the effect of the individual temperamental factors themselves.⁵⁰ Evidence for this type of interaction of temperament with other etiological factors has been provided by Owens *et al.*,⁵¹ who found that high levels of emotionality in children are linked to lower levels of responsiveness in mothers, which, in turn, may compromise the establishment of a secure attachment relationship. The lack of a secure attachment, then, could further enhance the risk of the development of internalizing/externalizing psychopathology.⁵²

The results of this study should be interpreted in light of some limitations. There was no data available to assess the psychopathology of mothers and their soothing practices toward their twins. Maternal psychopathology is considered a risk factor for obesity and internalizing/externalizing problem behaviors, and it may have an impact on maternal perception of offspring's behavior and temperament.⁵³⁻⁵⁷ Furthermore, we could not control for parental practices, which might as well be related to infants' temperament.⁵⁸ We had no data regarding breastfeeding

and maternal Type II diabetes mellitus, which have been found to be associated with children's temperament and behavior.^{59,60} Full control for the familiar socioeconomic status (SES) was not possible, since we lacked the data regarding parental income. Nonetheless, maternal level of education and employment status are considered the other two core components of SES⁶¹ and can provide a reliable indication of the familiar situation. Additionally, we were not able to account for the presence of other children in the family, which might have affected maternal ratings. Although previous studies did not observe an association between chorionicity and children's psychopathology,²³ we cannot exclude an uncontrolled effect of chorion type on our results. Finally, although self-reported height and weight are considered accurate enough and widely used in epidemiological studies, it was suggested that overweight and obese women are more likely to under-report their pre-pregnancy weight.⁶² Consequently, we cannot rule out an effect of biased reports on results.

In sum, the results of this study provide evidence that maternal pre-pregnancy BMI, which has been suggested as an important factor in emotional/behavioral problems, is not related with infants' temperament. These findings suggest that temperament is a complex constellation of characteristics with varying influences, as opposed to a unified, biologically driven system, as previously suggested. Additional studies are needed for elucidating the developmental paths of infant temperament and should consider not only maternal pre-pregnancy BMI but also maternal diet and physical health before and during pregnancy, as well as maternal temperament and psychopathology.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the University of Birmingham Ethics Committee.

Informed consent. Informed consent was obtained from all individual participants included in the study by the University of Birmingham Ethics Committee.

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