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# Interrelations Between Maternal Smoking During Pregnancy, Birth Weight and Sociodemographic Factors in the Prediction of Early Cognitive Abilities

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## Abstract

Maternal prenatal smoking, birth weight and sociodemographic factors were investigated in relation to cognitive abilities of 1544 children (aged 3.5 years) participating in the Québec Longitudinal Study of Children's Development. The Peabody Picture Vocabulary Test (PPVT) was used to assess verbal ability, the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) block design test to assess visuospatial ability, and the Visually Cued Recall (VCR) task to assess short-term memory. Prenatal smoking was related to performance on the WPPSI-R, the PPVT, and the VCR, although it did not independently predict any cognitive ability after maternal education was taken into account. Birth weight was a more robust predictor of all outcome measures and independently predicted VCR-performance. Birth weight interacted significantly with family income and maternal education in predicting visuospatial ability, indicating a greater influence of birth weight under relatively poor socio-economic conditions. Parenting and family functioning mediated associations between maternal education/family income and cognitive task performance under different birth weight conditions, although there were indications for stronger effects under relatively low birth weight. We conclude that investigations of moderating and mediating effects can provide insights into which children are most at risk of cognitive impairment and might benefit most from interventions.

### Keywords

nicotine; smoking; pregnancy; birth weight; cognitive; preschool

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## INTRODUCTION

Maternal smoking during pregnancy, low birth weight and poor sociodemographic conditions have all been associated with deficits in children's cognitive abilities (e.g. Breslau, Chilcoat, DelDotto, Andreski, & Brown, 1996; Fried, Watkinson, & Gray, 2003; Linver, Brooks-Gunn, & Kohen, 2002). Prenatal smoking and low birth weight are strongly associated with each other and both occur more frequently under disadvantageous socio-economic circumstances (Gazmararian, Adams, & Pamuk, 1996; Kramer, 1987; Magee, Hattis, & Kivel, 2004). However, the interrelations among prenatal smoking, birth weight and sociodemographic influences in the prediction of offspring cognitive abilities have not extensively been investigated.

The most frequently asked question regarding associations between prenatal smoking/birth weight and children's cognitive abilities is whether they are proxies for a wide range of other, mainly sociodemographic predictors of children's cognitive abilities. Both prenatal smoking (Batstra, Hadders-Algra, & Neeleman, 2003; Cornelius, Ryan, Day, Goldschmidt, & Willford, 2001; Fried *et al.*, 2003; Kristjansson, Fried, & Watkinson, 1989; Mortensen, Michaelsen, Sanders, & Reinisch, 2005; Olds, Henderson, & Tatelbaum, 1994; Sexton, Fox, & Hebel, 1990) and birth weight (across the entire spectrum of birth weight, ranging up to 4–4.5 kg) (Breslau *et al.*, 1996; Jefferis, Power, & Hertzman, 2002; Shenkin, Starr, & Deary, 2004) may be independent predictors of children's cognitive abilities, although reports have not been consistent. An increasing number of studies show that associations between prenatal smoking and offspring cognitive abilities are accounted for by specific sociodemographic factors such as parental IQ, parental education, SES, and family environment (Baghurst, Tong, Wood-ward, & McMichael, 1992; Breslau, Paneth, Lucia, & Paneth-Pollak, 2005; Fergusson & Lloyd, 1991; Lawlor *et al.*, 2006; MacArthur, Knox, & Lancashire, 2001; McGee & Stanton, 1994; Trasti, Vik, Jakobsen, & Bakketeig, 1999). Associations between birth weight and cognitive abilities appear more robust, although they are generally smaller than those of sociodemographic factors (e.g. Breslau *et al.*, 1996; Jefferis *et al.*, 2002; Shenkin *et al.*, 2004).

Prenatal smoking might affect children's cognitive abilities through its impact on birth weight. Metabolites of cigarette smoke act as vasoconstrictors limiting utero-placental blood flow (Suzuki, Minei, & Johnson, 1980). Consequently, the amounts of oxygen and essential nutrients reaching the foetus are significantly reduced, resulting in intrauterine growth retardation. Effects of prenatal smoking on birth weight have consistently been demonstrated (Kramer, 1987; Magee *et al.*, 2004). However, few reports have investigated the role of birth weight as a mediator of the association between prenatal smoking and children's cognitive outcomes. Breslau *et al.* (2005) and Mortensen *et al.* (2005) inferred the absence of a mediating effect based on the fact that associations between prenatal smoking and offspring IQ were only marginally attenuated after including birth weight in their regression models. However, no direct mediation tests were performed in these studies and the fact that associations between prenatal smoking and offspring IQ remained significant does not rule out the possibility of partial mediation by birth weight.

A related question, which also stems from the observed association between prenatal smoking and birth weight, is whether maternal smoking during pregnancy can explain associations between socio-economic factors and low birth weight (Kramer, 1987). Maternal smoking, like poor nutrition, drug and alcohol intake, might stand out among pregnancy behaviours that occur more often under poor socio-economic circumstances, and therefore account for associations between socio-economic factors and birth weight. Thus, associations between prenatal smoking and children's cognitive abilities may be accounted for by sociodemographic factors and birth weight. Alternatively, prenatal smoking and birth weight may actually interact with sociodemographic factors in the prediction of children's cognitive outcomes, i.e. the consequences of smoking during pregnancy or of low birth weight might be more serious under poor sociodemographic conditions. Conversely, we can postulate that a stimulating background could compensate for biological adversity. Although there are indications that effects of social and economic factors on cognition are greater in children with low birth weight (e.g. Brooks-Gunn, Gross, Kraemer, Spiker, & Shapiro, 1992), there is no clear-cut evidence for an interaction between birth weight and socio-economic factors. The possibility of prenatal smoking having a stronger effect on children's cognitive outcomes under poor socioeconomic circumstances has not been extensively studied either (see Olds, 1997).

Identifying interactions may be essential to further our understanding of the mechanisms by which prenatal smoking and/or low birth weight might be associated with offspring cognitive abilities (Breslau *et al.*, 2005). At a clinical level these interactions may help identify children who are most at risk for cognitive impairments. Under limited resources it seems best to target the most vulnerable children in interventions to improve cognitive abilities. Further, the best targets for interventions would be specific mediators of associations between more general indicators of socio-economic status, such as maternal education and family income, and children's cognitive outcomes (e.g. Tamis-LeMonda, Shannon, Cabrera, & Lamb, 2004). Such interventions could target family processes such as parenting and family functioning (e.g. Linver *et al.*, 2002). Studies showing mediating effects of family processes in associations between family income/maternal education and children's cognitive abilities have typically involved groups with increased vulnerability for cognitive impairment such as groups with low birth weight (e.g. Linver *et al.*, 2002). However, these studies have not investigated whether such mediating effects were specific to groups with low birth weight or prenatal smoking.

In summary, we will test the hypotheses that (1) sociodemographic factors account for associations between prenatal smoking and birth weight on the one hand, and early cognitive abilities on the other, (2) birth weight mediates associations between prenatal smoking and early cognitive abilities, (3) prenatal smoking accounts for associations between maternal education and family income on the one hand, and birth weight on the other, (4) prenatal smoking and birth weight interact with sociodemographic factors, in the prediction of children's early cognitive abilities, and (5) mediators of maternal education and family income, i.e. family functioning and parenting, are more influential under low birth weight or 'high' smoking conditions.

# METHODS

## Participants

The children of this study participate in the Québec Longitudinal Study of Children's Development, a prospective longitudinal study of children born between October 1997 and July 1998 in the province of Québec, Canada (Jetté and Des Groseilliers, 2000). In order to obtain a representative cross section of the population, a socio-economic and region-based stratification procedure was used. The sample plan excluded: (1) infants in the far North administrative region, Cree or Inuit regions, or living on aboriginal reservations; (2) infants for whom the duration of gestation could not be determined from the birth record; and (3) infants born at less than 24 weeks gestation and infants born at greater than 42 weeks gestation, the latter because of the delay in receiving and processing birth record data from hospitals. A total of 2223 families (75.6% of targeted population) participated in the study when the infant was aged 5 months between the months of March and November, 1998. Assessment of cognitive abilities first took place when the children were approximately 3.5 years of age ($M$ = 40.6 months, S.D. = 0.58, $n$ = 1950). Parental informed consent was obtained before every assessment and the protocol was approved by the Ethics Committee of the Institut de la Statistique du Québec.

## Measures

When the children were 5 months of age, mothers were asked about their smoking behaviour throughout pregnancy. To assess dose-dependency, mothers were classified into one of three groups (0, 1–9, or ≥10 cigarettes/day). A total of 1133 Mothers (73.4%) did not smoke during pregnancy, 186 mothers (12%) smoked 1–9 cigarettes/day, and 225 mothers (14.6%) smoked ≥10 cigarettes/day. A total percentage of 26.6 of mothers who smoked during pregnancy is common in present-day Western countries (cf. Batstra *et al.*, 2003; Breslau *et al.*, 2005). Birth weight and gestational age were derived from birth records. Birth weight for gestational age was standardized within gender for each week of gestation using recent Canadian norms (Kramer *et al.*, 2001). Five socio-demographic variables were included in the analyses. Family income and maternal education are variables that were shown to attenuate prenatal smoking and birth weight associations with offspring cognitive abilities in previous studies (e.g. Breslau *et al.*, 2005; Shenkin *et al.*, 2004; Trasti *et al.*, 1999). Two parenting measures (responsiveness and involvement) and a measure for family dysfunction were included because they were shown to mediate the maternal education and family income associations with offspring cognitive abilities (e.g. Linver *et al.*, 2002; Tamis-LeMonda *et al.*, 2004).

At the 5-month assessment, mothers provided information about household income (1 = less than 10 000$ CAN to 8 = more than 80 000$ CAN) and maternal education (1 = no high school diploma to 7 = university degree). The Home Observation for Measurement of the Environment (HOME)-Infant version (Caldwell & Bradley, 1984) was used to assess maternal responsiveness and maternal involvement at ages 5 and 17 months. The internal consistency values (Cronbach's $\alpha$) for the items of these scales were above 0.90. The items for responsiveness involve (mostly verbal) communication between parent and child. The items for involvement assess whether the parent provides the child with a stimulating learning environment. Family functioning at 5 and 17 months was scored by the mother using a 13 item 4-point Likert scale (strongly agree–strongly disagree), including items such as 'in times of crisis we can turn to each other for support', 'there are lots of bad feelings in our family', and 'we don't get along well together' (Statistics Canada, 1995). The variables were recoded in order for higher values to indicate greater dysfunction.

At age 3.5, children were assessed on three tasks: the Peabody Picture Vocabulary Test (PPVT) (Dunn & Dunn, 1981) to measure verbal ability, the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) block design test (Wechsler, 1989) to measure visuospatial ability, and the Visually Cued Recall task (VCR) (Zelazo, Jacques, Burack, & Frye, 2002) to measure short-term memory. For the PPVT, children had to select one of four pictures representing a word said to them by the experimenter. More difficult words were presented in later trials. For the WPPSI-R block design, children had to reproduce configurations of red and white coloured blocks. For the VCR the children had to remember a gradually increasing span of items shown on a card. The three tasks were all administered until a cessation criterion was met.

### Data Preparation

Of the 1950 potential participants at age 3.5 years, 1830 children completed the WPPSI-R block design test, 1795 children completed the PPVT, and 1768 children completed the VCR. The number of participants with a score on all three tasks, and scores for prenatal smoking, birth weight for gestational age, maternal education, family income, parenting measures and family dysfunction was 1544. Birth weight had a similar relation to task outcomes in children born prematurely (cut-off<37 weeks, $n = 71$) compared to the rest of the sample. Thus, all 1544 subjects were included in subsequent analyses. Scores were skewed towards the lower end of the distribution, and were normalized with square root transformation (Howell, 2002). All scores (independent and dependent variables) were standardized to facilitate interpretation and comparisons across tests.

### Statistical Analyses

First, in order to assess the separate influence of each of the five socio-demographic variables on associations between prenatal smoking and birth weight on the one hand, and offspring verbal ability, visuospatial ability and short-term memory on the other, a series of simple linear regression analyses were performed. Second, in order to assess interrelations among prenatal smoking, birth weight and sociodemographic factors (and to assess whether prenatal smoking and birth weight were robust against concurrent control for multiple sociodemographic factors) hierarchical multiple regression analyses were employed. Hierarchical multiple regression allows entering specific independent variables in an *a priori* order so that influences of variables entered later in the model can be ascertained over and above the influence of previously introduced variables. Thus, in this set of three regression analyses predicting, respectively, performance on WPPSI-R blocks, PPVT, and VCR, we entered prenatal smoking in a first block, birth weight in a second block, and all sociodemographic factors together in a third block. The stepwise procedure was employed in the third block because we had no *a priori* model of the relative strength of the factors in predicting cognitive outcome over and above the effects of prenatal smoking and birth weight. In addition, the strongest sociodemographic predictors of cognitive outcome may be different from the socio-demographic factors that most strongly attenuate associations between prenatal smoking/birth weight and children's cognitive abilities.

In order to test the second hypothesis, i.e. that birth weight is a significant mediator of the associations between prenatal smoking and cognitive outcome measures, we applied the Sobel Test (Sobel, 1982), using an interactive calculation tool by Preacher and Leonardelli (2001).

In order to test hypothesis number three, i.e. that prenatal smoking might account for associations of maternal education and family income with birth weight, two simple linear regression analyses were performed predicting birth weight from family income and prenatal smoking and from maternal education and prenatal smoking.

The fourth hypothesis, i.e. that prenatal smoking and birth weight interact with sociodemographic factors, was first tested with regression analyses using these predictors as continuous variables. When significant interactions were observed, categorical variables for the sociodemographic variables were created according to mean splits. If, in analyses of variance the interaction persisted with the categorical variable, strength and direction of associations between prenatal smoking/birth weight and outcome variables in the different sociodemographic groups were compared (see Howell, 2002).

The final set of analyses consisted of mediation tests to determine whether parenting and family functioning were stronger mediators of associations between maternal education/ family income and cognitive outcomes under high prenatal smoking and low birth weight conditions.

# RESULTS

## Attrition

First, a number of comparisons were made between families of children who were excluded from statistical analyses because they had dropped out of the study before they were 3.5 years old ($n = 273$, 12.3%) or had missing values on predictor variables or outcome measures ($n = 406$, 18.2%) and those who were included in statistical analyses ($n = 1544$, 69.5%). There were no differences regarding prenatal smoking and birth weight, but families of children excluded from the analyses had poorer scores on four of the five sociodemographic factors: family income ($t(2180) = 5.4$, $p<0.001$), maternal education ($t(2218) = 4.1$, $p<0.001$), responsiveness ($t(1959) = 5.3$, $p<0.001$), and family dysfunction ($t(2208) = -4.1$, $p<0.001$). Despite this non-random attrition, amongst families of children who were included in statistical analyses 24.6% ($n = 380$) scored in the lowest quartile of overall income distribution, 24.4% ($n = 377$) scored in the lowest quartile of the overall maternal education distribution, 22.9% ($n = 354$) scored in the lowest quartile for responsiveness, and 21.7% ($n = 335$) scored in highest quartile for family dysfunction.

### Prenatal Smoking, Birth Weight, and Sociodemographic Factors

Prenatal smoking was related to performance on the WPPSI-R blocks task [$F(1, 1542) = 8.7$, $p = 0.003$], the PPVT [$F(1, 1542) = 24.8$, $p<0.001$], and the VCR-task [$F(1, 1542) = 22.9$, $p<0.001$], all indicating a decrease in performance level with an increase in prenatal smoking. Birth weight significantly predicted performance on the PPVT [$F(1, 1542) = 6.8$, $p = 0.009$] and the VCR [$F(1, 1542) = 9.8$, $p = 0.002$], indicating better performance with increasing birth weight. Birth weight was not significantly associated with performance on the WPPSI-R block design task [$F(1, 1542) = 2.3$, $p = 0.126$]. All sociodemographic variables were significantly related to performance level in all tasks, except for family dysfunction which was not related to performance on the WPPSI-R blocks task (see Table 1).

As expected, prenatal smoking was significantly associated with all socio-demographic factors and birth weight (See Table 2). There were also low but significant positive associations of birth weight with family income ($r = 0.06$, $p = 0.012$) and maternal education ($r = 0.09$, $p<0.001$).

### Interrelations Between Prenatal Smoking, Birth Weight and Sociodemographic Factors

Simple linear regression analyses showed that prenatal smoking remained a significant predictor of performance on the PPVT ($\beta = -0.11$, $p<0.001$) and the VCR ($\beta = -0.08$, $p = 0.001$) after the introduction of family income, while it became non-significant as a predictor of performance on the WPPSI-R blocks task ($\beta = -0.04$, $p = 0.102$). After introduction of maternal responsiveness, prenatal smoking remained a significant predictor of performance on all tasks (WPPSI-R blocks: $\beta = -0.07$, $p = 0.006$; PPVT: $\beta = -0.11$, $p<0.001$; VCR: $\beta = -0.11$, $p<0.001$). Similar results were obtained after introduction of maternal involvement (WPPSI-R blocks: $\beta = -0.09$, $p = 0.006$; PPVT: $\beta = -0.11$, $p<0.001$; VCR: $\beta = -0.12$, $p<0.001$) and family dysfunction (WPPSI-R blocks: $\beta = -0.07$, $p = 0.004$; PPVT: $\beta = -0.12$, $p<0.001$; VCR: $\beta = -0.12$, $p<0.001$). However, maternal education accounted for the effects of prenatal smoking on performance of all tasks (WPPSI-R Blocks: $\beta = -0.01$, $p = 0.603$; PPVT: $\beta = -0.03$, $p = 0.322$; VCR: $\beta = -0.04$, $p = 0.104$). The simple regression analyses with birth weight and maternal education and with birth weight and family income showed that birth weight remained a significant predictor of PPVT-performance in the analysis with family income ($\beta = 0.05$, $p = 0.044$), but was no longer a significant predictor after control for maternal education ($\beta = 0.04$, $p = 0.118$). Birth weight did remain a significant predictor of VCR-performance in the analysis with family income ($\beta = 0.07$, $p = 0.007$) and in the analysis with maternal education ($\beta = 0.06$, $p = 0.021$).

Hierarchical regression analyses showed that the introduction of birth weight in the second step did not strongly attenuate the associations between prenatal smoking and cognitive outcomes (see Table 3). When birth weight was entered in the second block, there was only a significant increase in explained variance for the VCR ($R^2$-change = 0.003, $F(1, 1538) = 5.4$, $p = 0.021$). Results also indicated that prenatal smoking generally had a stronger association with cognitive outcome measures than birth weight. However, the introduction of sociodemographic factors in the third block of the regression analyses showed that associations between prenatal smoking and cognitive outcome measures were much less robust to the introduction of sociodemographic factors than associations between birth weight and intellectual outcome, and only the association between birth weight and VCR-performance remained significant. The stepwise procedure in block 3 of the hierarchical regression analyses also showed that maternal education was the first selected sociodemographic predictor for each task.

Mediation tests showed that birth weight was a significant mediator of the association between prenatal smoking and VCR-outcome ($z = -2.25$, $p = 0.024$), while it approached significance for the association between prenatal smoking and PPVT-outcome ($z = -1.77$, $p = 0.076$). Hypothesis number three was tested with simple regression analyses. The association between family income and birth weight was fully accounted for by prenatal smoking ($\beta$ family income = 0.03, $p = 0.284$ (compared to a $\beta$ of 0.06, $p = 0.012$, when there was no control for prenatal smoking); $\beta$ prenatal smoking = −0.17, $p<0.001$), as was the association between maternal education and birth weight ($\beta$ maternal education = 0.04, $p = 0.135$ (compared to a $\beta$ of 0.06, $p = 0.09$, when there was no control for prenatal smoking); $\beta$ prenatal smoking = −0.16, $p<0.001$). The association between prenatal smoking and birth weight hardly changed (from $\beta = -0.17$, $p<0.001$) when it was introduced in regression analyses together with family income or maternal education.

### Interactions

There were no significant interactions between prenatal smoking and socio-demographic factors in the prediction of cognitive outcome measures. In contrast, birth weight interacted significantly with family income in the prediction of WPPSI-R blocks performance ($\beta = -0.090$, $p<0.001$). In a follow up test, when family income was split at the mean (low income: $n = 637$; high income: $n = 907$), the interaction remained significant in analysis of variance [$F(1, 1540) = 9.8$, $p = 0.002$], and indicated that there was a stronger association between birth weight and WPPSI-R blocks score under low income conditions ($r = 0.131$, $p = 0.001$) compared to higher income conditions ($r = -0.034$, $p = 0.301$). Both the correlations ($z = 3.11$, $p<0.001$) and the slopes ($t = 3.16$, $p<0.01$) significantly differed for the two groups. There was also a significant interaction between birth weight and maternal education in the prediction of WPPSI-R blocks ($\beta = -0.056$, $p = 0.025$), which remained significant in analysis of variance using mean splits [$F(1, 1540) = 8.3$, $p = 0.004$]. The interaction indicated a stronger association between birth weight and WPPSI-R blocks performance under relatively low maternal education conditions ($n = 808$, $r = 0.100$, $p = 0.005$) compared to higher maternal education conditions ($n = 736$, $r = -0.049$, $p = 0.186$). The correlations between birth weight and cognitive outcome differed significantly between the two groups ($z = 2.93$, $p = 0.002$), as did the slopes ($t = 2.86$, $p<0.01$).

### Mediation Under Different Prenatal Smoking and Birth Weight Conditions

As shown in Table 3, maternal education and family income were independent predictors of each of the cognitive outcome measures. In line with previous studies (e.g. Linver *et al*., 2002; Tamis-LeMonda *et al*., 2004), responsiveness (PPVT: $z = 3.9$, $p<0.001$; VCR: $z = 2.4$, $p = 0.016$), involvement (PPVT: $z = 3.4$, $p<0.001$), and family dysfunction (PPVT: $z = 2.9$, $p = 0.004$; VCR: $z = 2.0$, $p = 0.048$) were all significant mediators of maternal education. Responsiveness (PPVT: $z = 3.9$, $p<0.001$; VCR: $z = 2.5$, $p = 0.012$), involvement (PPVT: $z =$

3.3, $p$<0.001; VCR: $z$ = 2.3, $p$ = 0.023) and family dysfunction (PPVT: $z$ = 2.9, $p$ = 0.004; VCR: $z$ = 2.0, $p$ = 0.042) were also significant mediators of family income. When two birth weight groups were created according to a mean split and mediation tests were repeated for each of two birth weight groups, the mediating effects were generally present for both groups, although some were significant only in the group with relatively low birth weight: involvement in the maternal education-VCR association: $z$ = 2.1, $p$ = 0.04 (compared to $z$ = 1.6, $p$ = 0.10 in group with above average birth weight); family dysfunction in the maternal education-PPVT association: $z$ = 2.8, $p$ = 0.006 (compared to $z$ = 1.9, $p$ = 0.06 in group with above average birth weight) and in the family income-VCR association: $z$ = 1.96, $p$ = 0.05 (compared to $z$ = 1.3, $p$ = 0.20 in group with above average birth weight). No such differences were observed for different prenatal smoking conditions.

## DISCUSSION

The results of this study showed that (1) maternal education accounted for associations between prenatal smoking and indicators of early cognitive abilities, (2) birth weight significantly mediated the association between prenatal smoking and short-term memory, (3) prenatal smoking accounted for associations between maternal education and family income on the one hand, and birth weight on the other, (4) birth weight interacted with family income and maternal education in the prediction of visuospatial ability, and (5) family functioning and parenting generally mediated associations between maternal education and family income and early cognitive abilities in children regardless of birth weight, although some effects were stronger for those with below average birth weight.

The finding that the introduction of maternal education completely attenuated all associations between prenatal smoking and cognitive outcomes is in agreement with results of a number of studies (Baghurst *et al.*, 1992; Breslau *et al.*, 2005; Fergusson & Lloyd, 1991; Lawlor *et al.*, 2006; MacArthur *et al.*, 2001; McGee & Stanton, 1994), although this is one of the few studies showing specific effects of maternal education (see also Lawlor *et al.*, 2006; Trasti *et al.*, 1999). The results contrast with those from other studies that showed that the associations remained significant after control for maternal education and other socio-demographic factors (e.g. Fried *et al.*, 2003; Mortensen *et al.*, 2005; Olds *et al.*, 1994; Sexton *et al.*, 1990).

In trying to reconcile these contrasting reports, we note that Sexton *et al.* (1990) found significant differences but only compared children of non-smokers to children of heavy smokers. When we compared the performance of similarly extreme groups in our study (heavy smoking defined as ≥10 cigarettes/day), the associations between prenatal smoking and cognitive outcome were again completely accounted for by maternal education. Like Mortensen *et al.* (2005), we also examined the possibility that smoking during particular trimesters of pregnancy would be predictive of cognitive outcome measures. However, associations were always attenuated towards non-significance after the introduction of maternal education, regardless of whether the mother smoked only during the first, second or third trimester or throughout pregnancy. We propose that inconsistencies between studies could be the consequence of differences in sociodemographic variation between the samples or of cohort effects. For example, we note that the Ottawa Pregnancy Prospective Study investigated a low-risk, predominantly middle class sample (Fried *et al.*, 2003) and the sample tested by Olds *et al.* (1994) consisted of families of predominantly poor, teenage, or unmarried mothers. Both could be considered relatively sociodemographically homogeneous. In contrast, greater sociodemographic variation was present within the larger population sample of our study, allowing maternal education in particular to have a greater statistical sensitivity. An additional explanation could be that the inconsistent results across different studies may be due to cohort effects: maternal smoking during pregnancy may have been much more common and less related to sociodemographic characteristics in earlier cohorts (e.g. Cornelius *et al.*, 2001; Mortensen *et al.*, 2005). Cohort effects need to be considered along with developmental effects. Thus, equating for age at testing, cohort effects may account for differences between studies. Similarly, equating for cohort, or using within cohort longitudinal designs, testing age of offspring may account for differences. Our study seems to replicate in a young sample findings reported with older samples (e.g. Breslau *et al.*, 2005; Fergusson & Lloyd, 1991; Lawlor *et al.*, 2006; MacArthur *et al.*, 2001). However, the relatively small but significant interactive and mediating effects we identified may become exacerbated over time without proper intervention.

The age of participants also limited the type (and complexity) of cognitive tasks that could be administered. Therefore, the absence of robust associations between prenatal smoking and measures of verbal and visuospatial ability and short-term memory does not rule out the possibility that robust associations may exist with other more sensitive and specific aspects of cognition. For example, several studies have shown lower autonomic arousal and vigilance levels in children of mothers who smoked during pregnancy (Horne, Franco, Adamson, Groswasser, & Kahn, 2004; Kristjansson *et al.*, 1989; Raine, 2002). Measures of arousal and vigilance might be specifically sensitive to prenatal smoking, because without continued nicotinic intake after birth, the increased number of nicotinic cholinergic receptor binding sites that have been formed as a consequence of in utero-nicotine exposure may be understimulated (Oncken *et al.*, 2003; Raine, 2002; Slotkin *et al.*, 2005).

An important consideration when appreciating these results is that the measure for prenatal smoking was based on mothers' self-reports at 5 months postpartum. Although it would have been ideal to obtain cotinine levels in such a large sample, the fact that prenatal smoking was strongly associated with birth weight makes it unlikely that there was significant underreporting of smoking during pregnancy. Our results do however indicate that prenatal smoking might influence cognitive development through birth weight, which, in accordance with other studies (Jefferis *et al.*, 2002; Shenkin *et al.*, 2004) did have a small but significant effect on short-term memory and was in general more robust to control for sociodemographic factors than prenatal smoking. Not only was the influence of socio-economic factors on birth weight fully accounted for by prenatal smoking, but birth weight was also a significant mediator of prenatal smoking in the prediction of short-term memory (and an almost significant mediator of the association between prenatal smoking and verbal ability).

We had a clear *a priori* rationale for choosing which variables to include in our analyses. Maternal education and family income were chosen because they were shown in previous studies to possibly account for associations between prenatal smoking/birth weight and offspring cognitive outcome, and parenting and family functioning were chosen because they might mediate associations between family income and maternal education and children's cognitive functioning. It could however be argued that under-control for other socio-demographic factors and prenatal exposure to alcohol and drugs may be a threat to the validity of some of our results. Thus, despite the fact that such analyses are beyond the focus of this study, we performed additional simple regression analyses predicting cognitive abilities from maternal depression, parental separation/divorce, maternal age, use of illegal drugs during pregnancy and alcohol consumption during pregnancy in addition to the variables that were already included in the original analyses. Like prenatal smoking, prenatal drug and alcohol use did not contribute significantly to the prediction of any of the cognitive outcomes after sociodemographic factors (particularly maternal education and family income) were taken into account. In contrast, birth weight remained a significant predictor of short-term memory ($\beta = 0.05$, $p = 0.034$).

This study innovates mainly by moving forward a research agenda designed to uncover mechanisms by which prenatal smoking and/or low birth weight might be associated with offspring cognitive abilities (Breslau *et al.*, 2005). A key finding is that sociodemographic factors interacted with birth weight. Birth weight was more strongly associated with WPPSI-R block design performance under lower family income and lower maternal education. Interactions between family income and birth weight were significant under a wide range of definitions of low income. The strongest correlation ($r = 0.284$, $p = 0.001$) between birth weight and WPPSI-R block design performance was observed when low family income was defined as <15 000$ CAN/year ($n = 136$). This amount corresponds to a yearly salary for an individual earning minimum wages, and would be roughly 50% below the poverty threshold for a 2-person family (Statistics Canada, 2006). Similarly, the interaction between maternal education and birth weight was significant under different definitions of low education, but the strongest association between birth weight and WPPSI-R block design performance was observed for those children whose mothers had no post-secondary education ($n = 157$, $r = 0.218$, $p = 0.006$).

From a clinical perspective, it is useful to look at relations between family income or maternal education and task performance when children fulfilled the diagnostic criteria for Low Birth Weight (LBW, <2500 g) or Intra-Uterine Growth Retardation (IUGR, a birth weight for gestational age in the lowest 10 percentiles of the population distribution). LBW ($N = 43$) did not interact with family income or maternal education in the prediction of task performance. IUGR interacted significantly (only) with family income in the prediction of WPPSI-R blocks performance [$F(1, 1540) = 7.4$, $p = 0.007$], indicating a much stronger correlation between family income and task performance for children with IUGR ($n = 149$, $r = 0.34$, $p<0.001$) compared to children with a higher birth weight for gestational age ($n = 1395$, $r = 0.14$, $p<0.001$). The correlations were significantly different ($z = 2.45$, $p<0.01$). There were no significant interactions between prenatal smoking and sociodemographic factors in the prediction of children's cognitive outcomes. As proposed by Breslau *et al.* (2005), the results of this study show that it is worthwhile to go beyond straightforward investigations of the socio-economic factors that may account for associations between prenatal smoking or low birth weight and cognitive abilities.

There may be other such interactions with family characteristics not covered in this study. Uncovering these would have practical implications first for identifying children most at risk of cognitive problems and second to determine on which aspect of the environment to intervene. The mediators of associations between family income or maternal education and children's cognitive outcomes may be useful in determining what environmental aspects could be targets in intervention programmes. Examples of such mediators are parenting style and quality, and family functioning. This study provides evidence that parenting and family functioning mediate associations between socio-economic factors and children's cognitive abilities regardless of birth weight, and also indicates the possibility that specific mediators may be particularly sensitive intervention targets in children with below average birth weight. We conclude that, because the effects of birth weight are more pronounced in children from poor sociodemographic backgrounds, these children should be targeted for interventions. Significant mediation effects indicate that these children may benefit from interventions involving parenting and family functioning.

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**Table 1**

Associations between sociodemographic factors and offspring cognitive outcome

| | WPPSI-R block design | | | | PPVT | | | | VCR | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Factors** | $F_{1,1542}$ | $\beta$ | $p$ | $R^2$ | $F_{1,1542}$ | $\beta$ | $p$ | $R^2$ | $F_{1,1542}$ | $\beta$ | $p$ | $R^2$ |
| Maternal education | 53.7 | 0.183 | <0.001 | 0.034 | 153.8 | 0.301 | <0.001 | 0.091 | 96.9 | 0.243 | < 0.001 | 0.059 |
| Family income | 39.6 | 0.158 | <0.001 | 0.025 | 110.3 | 0.258 | <0.001 | 0.067 | 60.6 | 0.194 | < 0.001 | 0.038 |
| Responsiveness | 6.9 | 0.067 | 0.009 | 0.004 | 46.3 | 0.171 | <0.001 | 0.029 | 15.7 | 0.100 | < 0.001 | 0.010 |
| Involvement | 7.3 | 0.069 | 0.007 | 0.005 | 32.6 | 0.144 | <0.001 | 0.021 | 10.4 | 0.082 | 0.001 | 0.007 |
| Family dysfunction | 1.2 | −0.028 | 0.267 | 0.001 | 23.6 | −0.123 | <0.001 | 0.015 | 11.9 | −0.088 | 0.001 | 0.008 |

Data courtesy of the Institut de la Statistique du Québec.

*Notes*: WPPSI-R block design: Wechsler Preschool and Primary Scale of Intelligence-Revised block design; PPVT: Peabody Picture Vocabulary Test; VCR: Visually Cued Recall.

## Table 2

Mean normalized scores of birth weight and sociodemographic factors by smoking during pregnancy category

| Number of cigarettes/day | 0 (*N* = 1133) | | | 1–9 (*N* = 186) | | | ≥10 (*N* = 225) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *M* | 95% CI mean | | *M* | 95% CI mean | | *M* | 95% CI mean | | $F_{2,1541}$ | *P* |
| | | Lower | Upper | | Lower | Upper | | Lower | Upper | | |
| Birth weight | 0.14 | 0.08 | 0.19 | −0.14 | −0.27 | −0.02 | −0.28 | −0.41 | −0.16 | 23.8 | <0.001 |
| Maternal education | 0.26 | 0.20 | 0.31 | −0.33 | −0.46 | −0.20 | −0.64 | −0.74 | −0.53 | 104.18 | <0.001 |
| Family income | 0.20 | 0.15 | 0.26 | −0.16 | −0.31 | −0.02 | −0.35 | −0.47 | −0.23 | 40.27 | <0.001 |
| Responsiveness | 0.08 | 0.03 | 0.13 | 0.06 | −0.07 | 0.18 | −0.13 | −0.24 | −0.03 | 6.25 | 0.002 |
| Involvement | 0.05 | −0.01 | 0.10 | 0.02 | −0.10 | 0.13 | −0.19 | −0.30 | −0.09 | 7.29 | 0.001 |
| Family dysfunction | −0.09 | −0.14 | −0.04 | 0.16 | 0.03 | 0.30 | 0.08 | −0.03 | 0.20 | 8.98 | <0.001 |

Data courtesy of the Institut de la Statistique du Québec.

*Note*: *M* = Mean normalized score.

**Table 3**

Hierarchical linear regressions: prediction of cognitive task performance by maternal smoking during pregnancy (MSP), birth weight, and sociodemographic factors

| Outcome variable | Independent variable(s) | *B* | SE | *β* | *p* |
|---|---|---|---|---|---|
| WPPSI-R blocks | | | | | |
| Block 1 | MSP | −0.10 | 0.033 | −0.075 | 0.003 |
| Block 2 | MSP | −0.09 | 0.034 | −0.070 | 0.006 |
| | Birth weight | 0.03 | 0.026 | 0.027 | 0.297 |
| Block 3 (stepwise)[a] | MSP | −0.01 | 0.035 | −0.006 | 0.826 |
| | Birth weight | 0.02 | 0.026 | 0.020 | 0.440 |
| | Maternal education | 0.13 | 0.029 | 0.136 | < 0.001 |
| | Family income | 0.09 | 0.029 | 0.087 | 0.003 |
| PPVT | | | | | |
| Block 1 | MSP | −0.17 | 0.034 | −0.126 | < 0.001 |
| Block 2 | MSP | −0.16 | 0.035 | −0.118 | < 0.001 |
| | Birth weight | 0.05 | 0.027 | 0.046 | 0.073 |
| Block 3 (stepwise)[b] | MSP | −0.01 | 0.035 | −0.006 | 0.805 |
| | Birth weight | 0.04 | 0.026 | 0.035 | 0.153 |
| | Maternal education | 0.21 | 0.029 | 0.208 | < 0.001 |
| | Responsiveness | 0.13 | 0.029 | 0.111 | < 0.001 |
| | Family income | 0.13 | 0.029 | 0.126 | < 0.001 |
| | Family dysfunction | −0.06 | 0.028 | −0.055 | 0.024 |
| VCR | | | | | |
| Block 1 | MSP | −0.17 | 0.035 | −0.121 | < 0.001 |
| Block 2 | MSP | −0.15 | 0.035 | −0.111 | < 0.001 |
| | Birth weight | 0.06 | 0.027 | 0.061 | 0.018 |
| Block 3 (stepwise)[c] | MSP | −0.04 | 0.036 | −0.028 | 0.296 |
| | Birth weight | 0.05 | 0.027 | 0.051 | 0.041 |
| | Maternal education | 0.18 | 0.030 | 0.176 | < 0.001 |
| | Family income | 0.09 | 0.030 | 0.088 | 0.002 |
| | Responsiveness | 0.07 | 0.030 | 0.058 | 0.021 |

Data courtesy of the Institut de la Statistique du Québec.

[a]Final model WPPSI-R blocks (Wechsler Preschool and Primary Scale of Intelligence-Revised block design): $F(4, 1536) = 16.2$, $p<0.001$, $R^2 = 0.041$, excluded variables: responsiveness, involvement, family dysfunction.

[b]Final model PPVT (Peabody Picture Vocabulary Test): $F(6, 1534) = 36.1$, $p<0.001$, $R^2 = 0.124$, excluded variable: involvement.

[c]Final model VCR (Visually Cued Recall): $F(5, 1535) = 24.0$, $p<0.001$, $R^2 = 0.072$, excluded variables: involvement, family dysfunction.