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RESEARCH ARTICLE

The Effect of Maternal Stress during Pregnancy on IQ and ADHD Symptomatology

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Abstract

Objective: Maternal stress during pregnancy (MSDP) has been linked to a decrease in Intelligence Quotient (IQ) in the general population. The purpose of this study is to first examine the association between MSDP and IQ in children with Attention-Deficit/Hyperactivity Disorder (ADHD) and second, to confirm, in a large sample, the link between MSDP and ADHD behavioral symptomatology. **Methods:** Four hundred ten children diagnosed with ADHD, ages six to 12, were consecutively recruited from the ADHD clinic and day hospital at the Douglas Institute from 1999 to 2013. IQ was assessed using the WISC III and IV. Symptom severity was evaluated using the Child Behavior Checklist (CBCL) and Connor's Global Index for Parents (CGI-P) and Teachers (CGI-T). **Results:** No significant effect of MSDP on full scale IQ was observed, but MSDP had a significant effect on CBCL and CGI scores. Elevated MSDP was significantly associated with increased CBCL internalizing scores (β=4.2, p<.01), CBCL externalizing scores (β=1.9, p=.04), CGI-P restless-impulsive scores (β=2.6, p=.01), CGI-P emotional lability scores (β=3.1, p=.02), and CGI-T restless-impulsive (β=2.2, p=.05) and emotional lability (β=3.4, p=.04) scores. MSDP increased the variance explained of ADHD symptomatology even after controlling for various factors (i.e. familial income, parental education, smoking and drinking during pregnancy, gender and age). **Conclusion:** The study demonstrates that in children with ADHD, MSDP does not have an impact on IQ but rather on ADHD symptomatology, highlighting the importance of potentially offering psychological and social support to mothers who experience stress during pregnancy.

Key Words: *maternal stress during pregnancy, ADHD, IQ*

Résumé

Objectif: Le stress maternel durant la grossesse (SMDG) a été lié à une diminution du quotient intellectuel (QI) dans la population générale. Cette étude vise d'abord à examiner l'association entre le SMDG et le QI chez les enfants souffrant du trouble de déficit de l'attention avec hyperactivité (TDAH) et deuxièmement, à confirmer, dans un vaste échantillon, le lien entre le SMDG et la symptomatologie comportementale du TDAH. **Méthodes:** Quatre cent dix enfants de 6 à 12 ans ayant reçu un diagnostic de TDAH ont été consécutivement recrutés dans la clinique du TDAH et l'hôpital de jour de l'Institut Douglas, de 1999 à 2013. Le QI a été évalué à l'aide des échelles WISC III et IV. La gravité des symptômes a été évaluée à l'aide de la liste du comportement de l'enfant (CBCL) et de l'index global de Conner pour les parents (CGI-P) et les enseignants (CGI-T). **Résultats:** Aucun effet significatif du SMDG sur le QI global n'a été observé, mais le SMDG avait un effet significatif sur les scores à la CBCL et au CGI. Un SMDG élevé était significativement associé à

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des scores d'internalisation accrus à la CBCL (β = 4,2; p<0,01), à des scores d'externalisation à la CBCL (β = 1,9; p = 0,04), à des scores agité-impulsif au CGI-P (β = 2,6; p = 0,01), à des scores de labilité émotionnelle au CGI-P (β = 3,1; p = 0,02), et à des scores agité-impulsif (β = 2,2; p = 0,05) et de labilité émotionnelle au CGI-T (β = 3,4; p = 0,04). Le SMDG augmentait la variance expliquée de la symptomatologie du TDAH même après contrôle de facteurs variés (c.-à-d., revenu familial, instruction des parents, tabagisme et consommation d'alcool durant la grossesse, sexe et âge). **Conclusion:** L'étude démontre que chez les enfants souffrant du TDAH, le SMDG n'a pas d'incidence sur le QI mais plutôt sur la symptomatologie du TDAH, ce qui souligne l'importance d'offrir potentiellement un soutien psychologique et social aux mères aux prises avec le stress durant la grossesse.

Mots clés: *stress maternel durant la grossesse, TDAH, QI*

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a widespread behavioral disorder affecting 8-12% of all school-aged children (Faraone, Sergeant, Gillberg, & Biederman, 2003). The disorder is characterized by difficulty with sustained attention, impulsivity and hyperactivity. These difficulties have a negative impact on their academic and social functioning (DuPaul & Jimerson, 2014), and occupational achievement later in life. The etiology of ADHD is complex. It has been shown that ADHD is a highly genetic disorder, with heritability estimates ranging from 71 to 90% (Faraone et al., 2005). This genetic susceptibility, in turn, interacts with environmental risk factors in a gene-environment interplay in which the end result is often ADHD (Thapar, Cooper, Jefferies, & Stergiakouli, 2012). These environmental factors include prenatal factors such as obstetrical complications (Linnet et al., 2006), smoking during pregnancy (Thakur et al, 2013) as well as postnatal factors such as psychosocial adversity and physical abuse (Thapar et al., 2012). Maternal stress during pregnancy (MSDP) is another factor that has been associated with ADHD (Grizenko, Shayan, Polotskaia, Ter-Stepanian, & Joober, 2008; Grizenko et al., 2012; O'Connor, Heron, Golding, Beveridge, & Glover, 2002).

The mechanism by which stress affects development is not entirely understood. The prevalent theory is the 'excess glucocorticoid' hypothesis, according to which the impact of stress on the offspring is mediated through the action of cortisol (Edwards, Benediktsson, Lindsay, & Seckl, 1993). Cortisol is a steroid hormone responsible for the body's adaptive response to stress. During pregnancy, the enzyme 11β-hydroxysteroid dehydrogenase type II (11β-HSD type II) deactivates cortisol in the placenta, ensuring that only small amounts cross over to the fetus. However, it is hypothesized that this enzyme may become saturated when the mother experiences severe stress, thereby allowing excess cortisol to reach the fetus (Charil, Laplante, Vaillancourt, & King, 2010).

Most of what is known today about the effect of MSDP and cortisol on brain development comes from animal studies. As reviewed by Weinstock (2008), studies have shown that MSDP slowed the acquisition of spatial memory in rats and mice, and was associated with decreased synaptic spine density in the hippocampus (Hayashi et al., 1998) and reduced hippocampal size in rodents (Szuran, Zimmermann, & Welzl, 1994; Schmitz et al., 2002) and non-human primates (Coe et al., 2003). Furthermore, synthetic cortisol has been shown to impair neural development in primates, with an overall 30% reduction in hippocampal volume (Charil et al., 2010; Uno et al., 1994).

In humans, MSDP has been studied in relation to Intelligence Quotient (IQ). IQ scores are obtained from standardized tests designed to measure overall intelligence. The IQ of a child is strongly associated with that of his parents (Neisser, 1996). However, other factors such as smoking during pregnancy (Clifford, Lang, & Chen, 2012) and socioeconomic status (Turkheimer, Haley, Waldron, D'Onofrio, & Gottesman, 2003) can affect the child's IQ, independently of genetics. Children with ADHD have been shown to have an IQ on average nine points lower than children without ADHD (Frazier, Demaree, & Youngstrom, 2004).

Two recent prospective studies reported that MSDP has a negative impact on child's IQ. A longitudinal study of children whose mother were pregnant during the 1998 Quebec Ice Storm revealed that children whose mothers experienced more severe objective but not subjective stress during pregnancy had lower full scale (FSIQ) and verbal IQ at age five and a half (Laplante, Drunet, Schmitz, Ciampi, & King, 2008). In a study looking at the impact of maternal state anxiety during pregnancy, it was reported that adolescents of mothers who were highly anxious during their pregnancy scored significantly lower on the vocabulary and block design subtests of the WISC-R (Van den Bergh et al., 2005).

Other prospective studies have looked at the relationship between prenatal maternal stress, anxiety and depression and scores on the Bayley scale for infant development (BSID), an instrument used to predict later intellectual ability (Bergman, Sarkar, O'Connor, Modi, & Glover, 2007). One group showed that pregnancy-specific anxiety, as well as high amounts of daily hassles, were associated with lower BSID scores at eight months of age (Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003). Another study showed that stressful life events during pregnancy were negatively correlated with BSID scores at fifteen and nineteen months of age (Bergman et al., 2007). Not all studies, however, have been straightforward in their findings. It appears that depending on how and when (i.e. which trimester) stress is measured and at what age the child is assessed, effects on infants' cognitive functioning may vary (Brouwers, van Baar, & Pop, 2001; Davis & Sandman, 2010). For example, Davis and Sandman (2010) reported that of all measures of prenatal maternal psychological distress they used, only pregnancy-specific anxiety significantly predicted BSID scores at age twelve months, but not at ages three and six months. Similarly, another study reported that state anxiety failed to predict BSID scores at twelve months of age but predicted lower scores at age two years (Brouwers et al., 2001).

Aside from its effect on IQ and BSID, MSDP has been associated with the development of ADHD symptoms in children. Prospective studies have shown that maternal stress during pregnancy is a predictor of ADHD symptoms (Rodriguez & Bohlin, 2005; Van den Bergh & Marcoen, 2004). In a study assessing learning and memory in six year olds, it was observed that MSDP predicted lower attention/concentration indexes (Gutteling et al., 2006). Another study reported that high antenatal anxiety is associated with hyperactivity and inattention in boys (O'Connor et al., 2002). According to McIntosh et al. (McIntosh, Mulkins, & Dean, 1995), children whose mothers experienced moderate stress during pregnancy are at higher risk of being diagnosed with an attention deficit disorder. Within the ADHD population, our group has shown that maternal stress during pregnancy is associated with more severe symptoms of ADHD (Grizenko et al., 2008), even when controlling for parenting style and environment (Grizenko et al., 2012). Similarly, in an Australian population cohort, MSDP was correlated with ADHD symptoms at age two while controlling for various confounders (Ronald, Pennell, & Whitehouse, 2011).

Children with ADHD constitute an at risk population for lower academic achievement, experiencing on average more difficulties with their schoolwork and increased risk of drop out (DuPaul & Jimerson, 2014). If children with ADHD who experienced severe MSDP have both more severe psychopathology and a lower IQ, they will form an even more at risk/sensitive subgroup. Thus, the purpose of the present study is two-fold; first, to examine the association between maternal stress during pregnancy and IQ in a clinical sample of ADHD children and second, to confirm the link between maternal stress during pregnancy and ADHD behavioral symptomatology that has been identified in previous studies using a larger sample.

Methods

Sample

Four hundred ten children aged 6-12 were recruited from the Disruptive Behavior Disorders day hospital and the children's outpatient clinic at the Douglas Mental Health University Institute in Montreal, Canada from 1999 to 2013. Children were referred to the clinic by their schools, social workers, general practitioners or pediatricians. Upon agreement of the child to participate, signed consent was obtained from the parents. All children were diagnosed with ADHD following the criteria established in the Diagnostic and Statistical Manual of Mental Disorder, Fourth edition (American Psychiatric Association, 2000) by an experienced child psychiatrist on the basis of school reports, observation of the child and an interview with the families. The Diagnostic Interview Schedule for Children Version IV (DISC-IV) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) was used to corroborate the diagnosis and assess comorbidities. Children with an IQ less than 70 were excluded. Diagnoses of autism, Tourette's disorder, or psychosis also constituted exclusion criteria.

Assessment

Parents filled a demographic questionnaire relating to socio-demographic and occupational information. Parental education was considered as the highest number of years either parent achieved. Children's IQ were measured at intake using the Wechsler Intelligence Scale for Children, Third Edition (WISC-III; Weschler, 1991) from 1999 to 2004 (n=195) and the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Weschler, 2003) from 2004 to 2013 (n=215). At the same time, obstetrical complications were evaluated with the Kinney Medical and Gynecological Questionnaire, a well-accepted interview administered to the mothers, which were then corroborated by medical records. The McNeil-Sjöström scale (McNeil & Sjöström, 1995) was used to assign a score of 1 to 6 to each complication, depending on its severity. Mothers who had one or more obstetrical complication scaled 4 or higher were considered as having had significant complications (e.g. gestational diabetes, prematurity, fetal distress).

During the same interview, mothers were asked about stressful life events that had occurred during their pregnancy. To corroborate and decrease recall bias, medical and obstetrical records were examined and a separate interview was held with a person who was close to the mother at the time of the pregnancy, such as her husband or her own mother, if possible. The information was then used to score maternal stress levels from 1 to 5 based on the DSM-III and DSM-III-R axis IV scales (1 = none, 2 = mild, 3 = moderate, 4 = severe and 5 = extreme). Subjects were divided into two categories: those whose mothers had undergone no or mild stress and those whose mothers had undergone moderate, severe or extreme stress. Examples of no or mild stress comprise moving to a new house or mild financial difficulty. Moderate or severe stressors included being physically abused, death of a parent or sibling, and separation from the spouse, for instance. Given that the information was collected retrospectively, stress was used as a dichotomous variable, so that it would be based on the presence or absence of major life events clearly identifiable by the mother.

To evaluate the children's ADHD symptoms, two different scales were used; the Conners' Global Index for Parents (CGI-P) and the Child Behavior Checklist (CBCL), both filled out by parents prior to intake. CGI-Teachers (CGI-T) were also filled out by the children's teachers. The CGI-P is a 10-item questionnaire used to evaluate child's behavior, which can be divided into two subscales: restless-impulsive and emotional lability (Conners, 2003). Finally, total CBCL scores (Achenbach, 1991), as well as internalizing and externalizing subscales, were also examined.

Data analysis

Demographic and clinical characteristics of our two stressor groups were compared using independent t-tests and χ^2. A hierarchical multiple linear regression model was then constructed to determine if MSDP, the variable of interest, and other covariates had an effect on full scale IQ (FSIQ). Covariates entered as a first step in the model were selected on the basis of their previous association with lower IQ or increased ADHD symptomatology: familial income, parental education, smoking and drinking during pregnancy, age, gender and obstetrical complications and test used to assess IQ (i.e. WISC-III or -IV). MSDP was then entered as a second step, and changes in variance explained were noted. Similar models were used to investigate the effect of MSDP on ADHD symptomatology, with CBCL and CGI-P or -T scores as dependent variables and the same covariates as above, with the exception of test used to assess IQ. Finally, since obstetrical complications did not significantly affect any of the outcomes studied, they were not entered in the final equations.

Results

Demographics

Table 1 shows the demographic characteristics of the two stressor groups. Children of mothers who were exposed to more stressful events during pregnancy came from families with lower income and a higher proportion of their mothers smoked while pregnant. Moreover, children of stressed mothers had significantly higher CBCL and CGI-P and -T total scores than children whose mothers were less stressed during their pregnancies ($p<0.001$, $p<0.001$, $p<0.01$, respectively). There was no significant difference in FSIQ, maternal alcohol use during pregnancy, number of obstetrical complications, gender, and age at baseline between the two groups.

FSIQ

Statistical analysis demonstrated that MSDP and gender had no significant effect on FSIQ (Table 2). Rather, it revealed that higher parental education (β=0.8, p<.01) higher household income (β=4.8, p<.01), and 3rd version of the WISC (β=4.8, p<.01) were significantly associated with higher child FSIQ in our model. These factors explained 12% of the variance, which value remained unchanged when MSDP was added to the equation. Similarly, MSDP was not found to influence verbal IQ nor performance IQ (data not shown).

ADHD behavioral symptomatology

Data analysis showed that MSDP had a significant effect on symptomatology according to CBCL and CGI-P total scores (both p<.01, Table 3 and 4). CBCL internalizing and externalizing scales were then investigated separately. Elevated MSDP (β=4.2, p<.01) and male gender (β=2.7, p=.03) were significantly associated with increased CBCL internalizing scores. The model including only covariates (income, parental education, smoking and drinking during pregnancy, age and gender) explained 5.0% of the variance in CBCL internalizing scores, and 8.7% when MSDP was added. High MSDP (β=1.9, p=.04), low income (β=5.3, p<.01), smoking during pregnancy (β=3.2, p<.01) were associated with higher CBCL externalizing scores. The model including only covariates explained 14.3% of CBCL externalizing scores variance, and 14.9% when MSDP was added. Likewise, MSDP was shown to have a significant effect on total CGI-P scores, which was then investigated using the two subscales. High MSDP (β=2.6, p=.01), female gender (β=6.8, p<.01) and younger age (β=0.8, p<.01) were associated with increased CGI-P restless-impulsive scores. MSDP (β=3.1, p=.02), female gender (β=5.2, p=<.01) and low income (β=3.7, p=.02) were associated with increased CGI-P emotional lability scores. The model including only covariates explained 9.9% of CGI-P restless-impulsive variance and 6.5% CGI-P emotional lability, and 11.0% and 7.5%, respectively, when MSDP was added. Finally, MSDP was shown to have a significant effect on total CGI-T scores (p=.03), which was then investigated using the two subscales. MSDP (β=2.2, p=.05) and female gender (β=5.0, p=<.01) were associated with increased CGI-T restless-impulsive scores, whereas MSDP (β=3.4, p=.04) and younger age (β=1.49, p=<.01) were associated with increased CGI-T emotional lability scores. The model including only covariates explained 4.3% of CGI-T restless-impulsive variance and 7.6% CGI-T emotional lability, and 5.0% and 8.4%, respectively, when MSDP was added.

Table 1. Demographic characteristics of subjects whose mothers underwent no/mild and moderate/high stress during pregnancy

Factor	No or mild stress N=211	Moderate or high stress N=199	t or χ^2	p
Child's age at baseline (SD)	9.0 (1.9)	9.1 (1.8)	0.4	.70
Gender. Female/Male	39/172	35/164	0.06	.81
Familial income ≤30 000$/>30 000$	55/156	101/98	26.5	<.001**
Maternal smoking during pregnancy. Yes/No	59/152	88/111	11.8	.001**
Maternal alcohol during pregnancy. Yes/No	48/163	44/155	0.02	.88
Obstetrical complications. Yes/No[a]	162/49	164/35	2.00	.16
FSIQ (SD)	98.6 (13.6)	96.2 (12.7)	1.9	.06
CBCL total (SD)	66.5 (8.2)	70.5 (8.3)	4.9	<.001**
CGI-P total (SD)	70.4 (10.6)	74.2 (11.1)	3.6	<.001**
CGI-T total (SD)	67.2 (12.4)	70.9 (11.7)	3.1	<.01**

SD= Standard Deviation

[a] Presence of obstetric complications defined as a rating of 4 or above on the McNeil-Sjöström scale
**Statistically significant at < .01

Table 2. Linear regression analysis of WISC full scale IQ in children with ADHD

	β	95% confidence interval		p
Child's age	-0.26	-0.92	0.41	.46
Child's gender	-1.57	-4.76	1.62	.33
Familial education	0.79	0.31	1.26	<.01**
Familial income	4.77	1.67	7.87	<.01**
Maternal smoking during pregnancy	-1.67	-4.51	1.18	.25
Maternal alcohol during pregnancy	1.35	-1.64	4.34	.38
WISC III or WISC IV	-4.80	-7.42	-2.17	<.001**
Maternal stress during pregnancy	-0.01	-2.56	2.55	1.00

**Statistically significant at < .01

Table 3. Linear regression analysis of Child Behavior Checklist (CBCL) scores in children with ADHD

	CBCL total				CBCL internalizing				CBCL externalizing			
	β	95% CI		p	β	95% CI		p	β	95% CI		p
Child's age	0.10	-0.32	0.52	.64	0.51	-0.01	1.03	.06	-0.39	-0.88	0.09	.11
Child's gender	-1.33	-3.32	0.66	.19	-2.73	-5.19	-0.27	.03*	-1.12	-3.42	1.19	.34
Familial education	-0.13	-0.42	0.17	.40	-0.14	-0.51	0.23	.45	-0.05	-0.39	0.29	.78
Familial income	-3.69	-5.57	-1.81	<.001**	-1.98	-4.31	0.34	.10	-5.31	-7.49	-3.13	<.001**
Maternal smoking during pregnancy	2.10	0.34	3.86	.02*	0.86	-1.32	3.04	.44	3.18	1.14	5.23	<.01**
Maternal alcohol during pregnancy	2.18	0.30	4.06	.02*	2.26	-0.06	4.58	.06	1.86	-0.32	4.03	.09
Maternal stress during pregnancy	2.59	1.00	4.18	<.01**	4.21	2.24	6.18	<.001**	1.90	0.05	3.74	.04*

95% CI = 95% CI of β
*Statistically significant at < .05
**Statistically significant at < .01

Table 4. Linear regression analysis of Conners' Global Index for Parents (CGI-P) scores in children with ADHD

	CBCL total				CBCL internalizing				CBCL externalizing			
	β	95% CI		p	β	95% CI		p	β	95% CI		p
Child's age	-0.66	-1.21	-0.11	.02*	-0.79	-1.31	-0.26	<.01**	-0.14	-0.82	0.55	.67
Child's gender	6.87	4.26	9.48	<.001**	6.84	4.38	9.32	<.001**	5.24	2.01	8.48	<.01**
Familial education	-0.28	-0.64	0.14	.21	-0.23	-0.60	0.14	.22	-0.26	-0.74	0.22	.30
Familial income	-2.45	-4.92	0.02	.05*	-1.80	-4.15	0.54	.13	-3.68	-6.74	-0.62	.02*
Maternal smoking during pregnancy	0.95	-1.37	3.27	.42	0.55	-1.66	2.75	.63	1.86	-1.02	4.72	.21
Maternal alcohol during pregnancy	0.10	-2.37	2.56	.94	0.49	-1.86	2.83	.68	-0.70	-3.76	2.35	.65
Maternal stress during pregnancy	2.92	0.83	5.01	<.01**	2.55	0.56	4.54	.01**	3.10	0.52	5.69	.02*

95% CI = 95% CI of β
*Statistically significant at < .05
**Statistically significant at < .01

Table 5. Linear regression analysis of Conners' Global Index for Teachers (CGI-T) scores in children with ADHD

	CBCL total				CBCL internalizing				CBCL externalizing			
	β	95% CI		p	β	95% CI		p	β	95% CI		p
Child's age	-0.93	-1.58	-0.28	<.01**	-0.39	-0.96	0.19	.19	-1.49	-2.35	-0.64	<.01**
Child's gender	2.86	-0.24	5.95	.07	5.05	2.33	7.78	<.001**	-2.00	-6.04	2.04	.33
Familial education	-0.24	-0.70	0.22	.30	-0.12	-0.52	0.29	.56	-0.55	-1.15	0.06	.08
Familial income	-2.21	-5.11	0.68	.13	-1.65	-4.20	0.90	.20	-2.78	-6.57	1.00	.15
Maternal smoking during pregnancy	1.76	-1.01	4.52	.21	0.85	-1.59	3.28	.49	2.67	-0.95	6.28	.15
Maternal alcohol during pregnancy	-1.03	-3.97	1.91	.49	-0.17	-2.75	2.42	.90	-2.35	-6.19	1.49	.23
Maternal stress during pregnancy	2.72	0.22	5.21	.03*	2.23	0.04	4.43	.05*	3.42	0.15	6.68	.04*

95% CI = 95% CI of β
*Statistically significant at < .05
**Statistically significant at < .01

Discussion

The purpose of our study was to deepen our understanding of the impact of maternal stress during pregnancy on children with ADHD. In our analysis, we in fact did not observe a significant contribution of MSDP on IQ. In this regard, our findings differ from those of Laplante et al. (2008) and of Van den Bergh et al. (2005), who both reported a negative impact of maternal stress during pregnancy on IQ. However, whereas these two studies looked at the effect of maternal stress during pregnancy in the general population, we looked at its effect in a high risk clinical population of children with ADHD, which might explain the difference between the observed tendencies. Other studies investigating the effects of MSDP on child development as measured by the BSID, reported that maternal stress during pregnancy was negatively correlated with BSID (Buitelaar et al., 2003; Davis & Sandman, 2010). However, most of these studies investigated different stressors (pregnancy-related anxieties or daily hassles) from what we observed in our sample. In our study, MSDP relates more to stressful events during pregnancy, such as being physically abused or losing a home in a fire. This, along with the fact that we tested this hypothesis in an ADHD population, may explain why our findings diverge.

On the other hand, our findings are similar to those reported by DiPietro who, after controlling for maternal education, gender and postnatal psychiatric measures, found that prenatal maternal perceived stress and prenatal maternal stress were not correlated with BSID (DiPietro, Novak, Costigan, Atella, & Reusing, 2006). Moreover, Davis and Sandman reported that state anxiety, perceived stress and depression during pregnancy were not correlated with child development in their model, only pregnancy-specific stressors were (2010).

What affected IQ was not MSDP but familial education, income and whether WISC-III or -IV was used. The latter might be attributable to the fact that we initially had more cases from lower socioeconomic background. By the time we started using the WISC-IV, the population served by our clinic diversified, and families tended to come from higher SES.

The second part of our hypothesis predicted that children whose mothers were severely stressed during their pregnancy would have more severe ADHD symptoms than those whose mothers were not stressed during their pregnancy. An important strength of the present study is that many variables that have been hypothesized to influence IQ or ADHD symptomatology were entered as covariates in our analysis. While controlling for these covariates, we still observed that children of moderately or severely stressed mothers show higher CBCL, CGI-P and CGI-T scores than those whose mothers were subjected to no or mild stress. This study thus confirms our earlier findings, but in a larger sample (N=410 vs. N=203 in 2008 (Grizenko et al.) and N=305 in 2012 (Grizenko et al.).

Limitations

The major limitation of our study was that many of our measures relied on mothers' recall. We, however, implemented ways of minimizing the potential effect of poor recall and/or recall bias. First, concerning stressful events during pregnancy, an interview was held with someone close to the mother who was asked to corroborate the events reported when possible. Second, stressors classified as moderate or severe were objective life events clearly identifiable by the mother. Finally, there is a possibility that shared methods variance may lead to an inflation of the association, as mothers report both their stress during pregnancy and their children's symptoms. However, since the association with stress was also observed on symptoms reported by teachers, this effect would be limited.

Conclusion

In conclusion, our study shows that in our ADHD population, maternal stress during pregnancy did not have an impact on IQ, but rather influenced ADHD symptomatology. Clinically, these findings illustrate the importance of identifying mothers who live deeply stressful events during their pregnancies in order to potentially offer psychological and social support as part of their prenatal care.

To understand the mechanisms underlying the effects of maternal stress during pregnancy, our group is planning to study epigenetic alterations in the offspring's genome. These include DNA modifications such as DNA methylation and acetylation of structural proteins (histones) that influence the transcription of a gene. Following this theory, for a same genotype, one could observe different phenotypes depending on the presence or absence of DNA modification, a process that is driven by environmental factors. For instance, using a rat model, a study demonstrated that offspring whose mothers were subjected to high prenatal stress levels had a significant decrease in DNA methylation in the frontal cortex and hippocampus compared to those whose mothers were subjected to lower stress levels (Mychasiuk, Ilnytskyy, Kovalchuck, Kolb, & Gibb, 2011). This suggests that maternal stress during pregnancy constitutes one of the factors that could cause epigenetic modifications. It may be that children with ADHD carry certain genes that are particularly vulnerable to methylation when exposed to certain environmental factors, which would present itself as increased symptoms of ADHD rather than a lower IQ. Clearly, a lot more research needs to be conducted in this area, but the field offers promising insight into understanding the effect of different environmental factors on cognition and behavior in children with ADHD.

Acknowledgements/Conflicts of Interest

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