Prenatal Effects of Selective Serotonin Reuptake Inhibitor Antidepressants, Serotonin Transporter Promoter Genotype (SLC6A4), and Maternal Mood on Child Behavior at 3 Years of Age

Tim F. Oberlander, MD, FRCPC; Michael Papsdorf, PhD; Ursula M. Brain, BA; Shaila Misri, MD; Colin Ross, PhD; Ruth E. Grunau, PhD

Objectives: To investigate whether prenatal selective serotonin reuptake inhibitor (SSRI) antidepressant exposure affects behavior in 3-year-olds of antenatally anxious or depressed mothers and whether risk was moderated by the serotonin transporter promoter (SLC6A4) genotype.

Design: Prospective longitudinal cohort design.

Setting: Vancouver.

Participants: Mothers and their 3-year-old children (n=33 SSRI exposed and n=42 nonexposed).

Main Exposures: Prenatal exposure to SSRI antidepressants and prenatal and postnatal maternal mood disturbances.

Main Outcome Measures: Parent report of child behavior (Child Behavior Checklist, ages 1.5-5 years) and the child SLC6A4 genotype. The covariates used were maternal mood during the third trimester, 3 months post partum, and at the 3-year follow-up study and the child’s 5-minute Apgar score.

Results: Prenatal exposure to both maternal depressed mood and SSRI antidepressants were associated with increased internalizing behaviors during early childhood, whereas current maternal mood increased risk for externalizing behaviors. Increased child anxiety and depression symptoms were predicted by higher third-trimester maternal anxiety only in children with 2 short S alleles. In contrast, increased aggression and externalizing behaviors were predicted by third-trimester maternal anxiety only in children with 2 copies of the L allele.

Conclusions: Exposure to prenatal SSRIs and maternal mood had distinct effects on child behavior at 3 years of age, reflected in an increased level of internalizing behaviors. The impact of antenatal maternal anxiety on child mood was moderated by the child SLC6A4 genotype. Despite SSRI treatment for prenatal maternal mood disturbances, childhood behavior at 3 years of age remained at risk.


EXPOSURE TO MATERNAL MOOD disturbances during pregnancy may be one of life’s first adverse experiences that potentially sets a course of increased risk of childhood behavioral disturbances.1-4 In animal models, gestational stress is associated with behavioral disturbances and altered stress regulation in offspring.5-7 Similarly, in clinical studies,5,8 prenatal maternal mood disturbances set up developmental trajectories that affected cognitive, behavioral, and emotional outcomes throughout childhood, even when controlling for obstetric risk, psychosocial disadvantage, and postnatal maternal mood. Antenatal anxiety doubles the risk of hyperactivity and conduct and emotional problems during early childhood and school age.9 Together, such early adverse experience has a “fetal programming” effect on the developing brain.10 The magnitude of the effect is clinically significant, with approximately 15% of emotional behavioral problems in childhood attributable to antenatal anxiety.11

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Antenatal mood disorders are increasingly being managed with selective serotonin reuptake inhibitor (SSRI) antidepressants, which are prescribed with an

Author Affiliations: Early Human Experience Unit, Developmental Neurosciences and Child Health, and Department of Pediatrics (Drs Oberlander, Papsdorf, and Grunau and Ms Brain), and Centre for Molecular Medicine and Therapeutics (Dr Ross), Reproductive Mental Health, Department of Psychiatry, University of British Columbia, Vancouver (Dr Misri), British Columbia, Canada.
expectation that pharmacotherapy for maternal mood disturbances will “buffer” the developing child from the effects of maternal mental illness. Alternatively, because these medications alter central serotonergic (serotonin) tone during early brain growth, they may also contribute to developmental risk. Primarily, SSRIs act by blocking the serotonin transporter (5-HTT), consequently increasing extracellular serotonin levels. Because SSRIs readily cross the placenta and the blood-brain barrier, maternal SSRI treatment alters central serotonin signaling of the fetus. Under-treated antenatal maternal mood disturbances also alter neonatal serotonin levels, leaving critical questions unanswered about how the effects of prenatal SSRI exposure differ from the impact of the underlying maternal disorder.

Long before serotonin acts as a neurotransmitter, it has critical roles as a trophic factor directing neuronal growth. It is conceivable that altered serotonin levels during development affect subsequent serotonergic function and vulnerability to affective disorders. Genetically modified mice lacking the serotonin transporter (SERT), analogous to an SSRI-induced increase in intrasynaptic serotonin, are at increased risk for depressed and anxious behaviors in adulthood, suggesting links between early disrupted serotonergic function and subsequent behavioral disturbances. SERT, one of the key regulators of serotonin neurotransmission, is the membrane-bound 5-HTT protein that governs the reuptake of serotonin from the synaptic cleft, returning it to the presynaptic neuron. Altered 5-HTT and reduced serotonin levels have been associated with depression, and the function of this protein is closely tied to polymorphisms in the serotonin transporter gene (SLC6A4) promoter region (SLC6A4 OMIM21 182138; 5-HTT). Differences in transporter-dependent reuptake efficiency are related to 44-base pair (bp) insertion/deletion polymorphisms in a region of repetitive sequence in the proximal 5′ regulatory region in the promoter region of the SLC6A4 gene, leading to differential transporter gene expression and clinical differences in SSRI efficacy. The short (S) variant is associated with reduced transcription of SLC6A4 and approximately 50% reduction in serotonin reuptake compared with the long (L) variant. The II genotype is associated with increased SSRI efficacy compared with the ss genotype, although effects have been inconsistent. Individuals with 2 copies of the short allele of the serotonin transporter promoter, a condition associated with reduced SERT expression, have increased vulnerability to depression and other mood disorders after stressful events in early life. In SSRI-exposed neonates, risk of neonatal neurobehavioral disturbances may be moderated by reduced serotonin transporter (SHTT or SERT) expression (SLC6A4 genotype), however, this single polymorphism does not seem to account for all outcomes.

Beyond the newborn period, little is known about the impact of prenatal SSRI exposure on child development. For the most part, childhood behaviors seem to be best predicted by current levels of maternal mood and not by prenatal SSRI exposure; however, findings have been limited by the difficulty in accounting for prenatal and postnatal maternal mental health. Increased externalizing symptoms were observed in SSRI-exposed 4-year-olds with increased cord SRR drug levels and a history of neonatal withdrawal behaviors, suggesting possible sustained links between fetal SSRI exposure and childhood neurobehavior. Altered serotonin levels during early periods of brain development, possibly via prenatal SSRI exposure or genetic variations that modify serotonin transport, may change serotonin-related neurobehavioral development.

This study was undertaken to examine associations between prenatal SSRI exposure and behavioral outcomes in early childhood controlling for prenatal and postnatal maternal mood. A secondary objective sought to examine whether such risk was moderated by the child SLC6A4 genotype, reflecting genetic variations in the capacity to control the severity of serotonergic tone. We expected that prenatal SSRI exposure, especially combined with 2 copies of the short S allele (thereby reducing SLC6A4 transcription and transporter activity), would increase the risk of behavioral disturbances in early childhood.

METHODS

PARTICIPANTS

With approval from the University of British Columbia Research Ethics Board and the Children’s and Women’s Health Centre of British Columbia Research Review Committee, and after receiving informed parent consent, we prospectively recruited a convenience sample of 98 mothers late in their second trimester (mean [SD], 24.2 [5.1] weeks) as part of a longitudinal study of the effects of antenatal SSRI exposure. Mothers were physician- and self-referred from the Reproductive Mental Health Clinic at British Columbia Women’s Hospital & Health Centre, a tertiary care referral service, community midwife clinics, and family physician practices in the greater Vancouver metropolitan area. All SSRI-treated mothers started taking medication based on clinical need, had a diagnosis of a mood disorder, and were already taking antidepressant medications at the time of conception. The criterion for recruitment was the presence or absence of SSRI antidepressant treatment rather than a threshold for mood symptoms. Women in the non-SSRI group were recruited from family or midwifery practices and had a range of mood symptoms (mean [SD] Hamilton Rating Scale for Depression [HAMD] score, 5.6 [6.8]) at the time of recruitment. Cord and third-trimester maternal blood samples were obtained for DNA analysis. Of the original 98 pregnant mothers recruited, 4 withdrew before the baby was born, leaving 94 newborns in the longitudinal study. Four more children then withdrew from the study before the end of the first year of life, and an additional 15 children were unavailable for the 3-year study (11 families moved and could not be contacted, and 4 mothers refused consent to participate). At the 3-year follow-up visit, 75 children returned (33 children of depressed mothers treated with an SSRI during pregnancy and 42 children of non-SSRI–treated mothers). Mothers had been treated with 1 of 5 SSRIs, which included SSRIs and serotonin norepinephrine reuptake inhibitors. For simplicity, the SSRI nomenclature is used. None of the mothers had taken other serotonergic medications or any other psychotropic or antidepressant medications during pregnancy.

SLC6A4 GENOTYPING

Genomic DNA was extracted from whole venous blood using the Flexigene DNA Blood Kit (Qiagen, Valencia, California). The L and S alleles of SLC6A4 were identified as previously described. Polymerase chain reaction was performed with oligonucleotide primers flanking the polymorphism (correspond-
were used in analyses. The CBCL also yields a total problem score, externalizing and internalizing scores, and subscale scores (emotionally reactive, depressed/anxious, withdrawn, somatic complaints, sleep problems, attention, and aggression). Scale scores were used in analyses. The CBCL also yields $T$ scores, with the mean (SD) set at 50 (10). $T$ scores were reported because of their widespread clinical application, and they were used only for descriptive purposes. Raw untransformed scores were used in the primary analyses.

## MATERNAL MOOD

Maternal mood was assessed during the third trimester of pregnancy, a mean of 33.7 weeks’ gestation, and again 3 months post partum using 4 instruments. During the pregnancy and 3 months post partum, the HAMD, a 14-item clinician-rated measure of anxiety with a score ranging from 0 to 56 (minimal to severe levels), were used. At the time of the 3-year follow-up study, maternal mood was assessed using the Beck Depression Inventory, a 21-question multiple-choice self-report inventory for measuring depression with scores ranging from 0 to 63, and the Beck Anxiety Inventory, a 21-question multiple-choice self-report inventory used for measuring severity of anxiety during the last week with scores also ranging from 0 to 63. Total scores were used in the analyses.

### STATISTICAL ANALYSIS

Analyses were undertaken in 2 stages. In the first stage, analyses of covariance were used to examine group (SSRI-exposed vs nonexposed) differences in child behavior using measures of prenatal (third-trimester) and postnatal (3-month and 3-year) maternal mood and neonatal risk (5-minute Apgar score) as covariates. Measures of maternal anxious and depressed mood were used in separate models. Because maternal mood measures varied between groups and during the antenatal and postpartum periods, they were used as continuous covariate measures. In the second stage, similar analytical models (analyses of covariance) were used to examine interactions between exposure group and SLC6A4 genotype (ss, sl, and ll), testing the role of genotype as a possible moderator of the effects of prenatal exposure on behavior. In this stage, measures of prenatal (third-trimester) and postnatal (3-month and 3-year) maternal mood and neonatal risk (3-minute Apgar score) were used as covariates. We calculated effect sizes ($\eta^2$) to examine the strength of these associations because the statistical significance of the findings would be affected by sample size and potentially by multiple comparisons.

### MATERIAL AND CHILD CHARACTERISTICS

Except for mood symptoms, educational level, and antidepressant medication use, maternal characteristics did not vary significantly between groups ($P > .05$) (Table 1 and Table 2). The SSRI-treated mothers had approximately 2.5 fewer years of higher education ($F = 9.1$, $P = .03$, $\eta^2 = .09$). Levels of maternal depression and anxiety symptoms during pregnancy and at 3 months post partum were 2 to 3 times higher in the SSRI-treated group than in the non-SSRI group ($P < .001$ for all), and they remained so 3 to 4 years post partum ($P < .05$ for all). All of the mothers took a prenatal vitamin containing the prenatal folic acid dose (0.8-1.0 mg). At the time of the 3-year study, most mothers in the prenatal SSRI-treated group were still taking medication, and 4 of the nonprenatally treated mothers had begun to take an SSRI (Table 2). Mothers in both groups were equally concerned about their child’s development, and none of the children were taking psychotropic medications at the time of the study. No interactions between time and group for any measure were observed ($P > .05$ for all) (Table 3). At 3 years, 78% of SSRI-exposed and 79% of nonexposed children who had been studied as neonates returned for this follow-up study. Child characteristics did not differ significantly between those who were studied at 3 years and those who were not studied ($P > .05$) (Table 4).

### TABLE 1. MATERNAL CHARACTERISTICS

<table>
<thead>
<tr>
<th>Variable</th>
<th>SSRI Exposed</th>
<th>Non SSRI Exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age at birth, mean (SD), y</td>
<td>31.9 (4.6)</td>
<td>33.3 (5.1)</td>
</tr>
<tr>
<td>Maternal education, mean (SD), y</td>
<td>15.3 (2.4)</td>
<td>18.0 (3.2)</td>
</tr>
<tr>
<td>Cigarettes/smoking, yes/no, No.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alcoholic drinks during pregnancy, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>67</td>
<td>51</td>
</tr>
<tr>
<td>1-10</td>
<td>24</td>
<td>42</td>
</tr>
<tr>
<td>&gt;10</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Cesarean delivery, %</td>
<td>36</td>
<td>31</td>
</tr>
<tr>
<td>Maternal SLC6A4 genotype, No.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ll</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>ls</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>ss</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>SSRI third-trimester dose, median (range), mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine (n=15)</td>
<td>20 (2-45)</td>
<td>NA</td>
</tr>
<tr>
<td>Fluoxetine (n=4)</td>
<td>30 (10-40)</td>
<td>NA</td>
</tr>
<tr>
<td>Sertraline (n=5)</td>
<td>50 (25-175)</td>
<td>NA</td>
</tr>
<tr>
<td>Venlafaxine (n=3)</td>
<td>75 (38-150)</td>
<td>NA</td>
</tr>
<tr>
<td>Citalopram (n=6)</td>
<td>25 (20-40)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; SSRI, selective serotonin reuptake inhibitor.

*P < .05.  
DNA samples from 2 SSRI-exposed and 1 nonexposed mother were unavailable for genotyping.

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SLC6A4 genotype ratios were distributed according to Hardy-Weinberg equilibrium for all 140 participants (68 children and 72 mothers; 7 child and 3 maternal samples were of poor quality and were not analyzed) together (allele frequency—children: L = 57.3% and S = 42.7%; maternal: L = 56.3% and S = 43.8%; and genotype frequency—child: ll = 32.4%, ls = 50.0%, and ss = 17.6%; maternal: ll = 33.3%, ls = 45.8%, and ss = 20.8%) and for mothers and infants separately (Tables 1 and 3). The allele frequency and genotype distribution was not different between SSRI-exposed and nonexposed mothers. Mean daily dose and length of prenatal SSRI exposure did not vary significantly between genotypes (P > .05).

**MODEL 1: CHILD BEHAVIORAL OUTCOMES**

**Internalizing Behaviors**

Higher internalizing scores were associated with prenatal SSRI exposure and increased levels of maternal anxiety at the time of the 3-year study (F = 3.978, P = .05, η² = 0.06 and F = 4.517, P = .04, η² = 0.07, respectively), controlling for third-trimester anxiety (HAMA) scores, 5-minute Apgar scores, and 3-month postpartum HAMA scores (Table 5). When controlling for prenatal and postnatal maternal depressed mood (HAMD) and 5-minute Apgar scores in a separate model, higher levels of internalizing symptoms were predicted by higher levels of maternal depression symptoms 3 years post partum (F = 5.816, P = .02, η² = 0.08) but not by prenatal SSRI exposure (F = 3.396, P = .07, η² = 0.05).

**Externalizing Behaviors**

Increased levels of externalizing behaviors were also associated with 3-year postpartum levels of maternal anxiety (Beck Anxiety Inventory) and depression symptoms (Beck Depression Inventory) using prenatal and postnatal HAMA and HAMD measures (in separate models) and 5-minute Apgar scores as covariates (F = 4.562, P = .04, η² = 0.07 and F = 6.75, P = .01, η² = 0.11 for Beck Anxiety Inventory/HAMA and Beck Depression Inventory/HAMD, respectively). Neither prenatal SSRI exposure nor maternal years of education contributed to externalizing symptoms in either model (P > .25) (Table 5).

**CBCL Subscale Scores**

Of the internalizing behavior subscales, prenatal SSRI exposure predicted increased levels of somatic complaints (F = 8.7, P < .01, η² = 0.12) and sleep disturbances (F = 4.8, P = .03, η² = 0.07). Increased maternal anxiety at the time of the 3-year study predicted child somatic (F = 7.918, P < .01, η² = 0.11) and emotionally reactive (F = 5.8, P = .02, η² = 0.08) symptoms. Similarly, in separate models, increased levels of maternal depressed mood at 3 years predicted increased emotionally reactive symptoms (F = 5.7, P = .02, η² = 0.08), whereas withdrawal behaviors were not associated with prenatal SSRI exposure or maternal mood (P > .05). Externalizing subscale scores (aggression and attention)
were not associated with prenatal SSRI exposure or measures of maternal mood ($P > .05$).

**MODEL 2: EFFECT OF THE CHILD SLC6A4 GENOTYPE**

When the child SLC6A4 genotype was added to the model, significant interactions with maternal third-trimester measures of mood emerged. Increased externalizing symptoms at 3 years were predicatd by an interaction between third-trimester maternal anxiety and the child SLC6A4 genotype ($F = 3.954$, $P = .03$, $\eta^2 = 0.13$). In particular, higher externalizing symptoms ($F = 5.945$, $P = .03$, $\eta^2 = 0.30$) and increased aggressiveness ($F = 4.97$, $P = .04$, $\eta^2 = 0.26$) were predicted by higher third-trimester maternal anxiety only in children with 2 long alleles (II) (Figure 1).

Increased child anxiety and depression symptoms were predicted (in separate models) by the interaction between both third-trimester maternal anxiety and depression symptoms and the child SLC6A4 genotype ($F = 5.055$, $P < .01$, $\eta^2 = 0.19$ and $F = 6.328$, $P < .01$, $\eta^2 = 0.20$, respectively). Specifically, increased child anxiety and depression symptoms were predicted by higher third-trimester maternal anxiety and depression symptom scores only in children with 2 short alleles (ss) ($F = 7.128$, $P = .04$, $\eta^2 = 0.54$) (Figure 2). No interactions were noted between child genotype and SSRI exposure in either model.

Child behavior and prenatal maternal anxiety were not associated in children with 1 long and 1 short allele ($F = 0.048$, $P = .83$, $\eta^2 = 0.002$ for anxious/depressed behavior; $F = 0.324$, $P = .57$, $\eta^2 = 0.011$ for aggressive behavior). Neither child sex nor maternal SLC6A4 genotype affected behavioral symptoms.

**COMMENT**

Prenatal SSRI exposure and higher current maternal anxiety contributed to increased internalizing behaviors in 3-year-old children. Increased levels of externalizing behaviors were also observed, but they were associated with current levels of 3-year postpartum maternal mood. Beyond the effects of prenatal exposure to SSRIs and maternal mood, the child SLC6A4 genotype moderated the impact of exposure to third-trimester maternal mood.

The SSRIs are often used to manage antenatal mood disturbances11 with the expectation that they optimize ma-
ternal mental health, thereby reducing child behavioral risk. However, child behavioral disturbances were still observed at 3 years even after prenatal and postpartum SSRI treatment, suggesting that such maternal antidepressant therapy did not buffer the children from the ongoing effects of maternal mood disturbances. Although maternal education differed between exposure groups, this did not contribute to child behavioral outcomes.

Children with poor or inefficient transcription of SLC6A4 (ss genotype), resulting in reduced levels of serotonin transporter protein and potentially reduced serotonin reuptake, coupled with third-trimester exposure to maternal anxiety, were seen as more anxious or depressed by their mothers, even controlling for prenatal SSRI exposure, perinatal risk, and postnatal (3-month) and 3-year postpartum maternal mood. This may reflect an effect related to increased intrasynaptic prenatal serotonin exposure and receptor sensitivity at critical periods of development, consistent with an extreme manipulation in central serotonin using a SLC6A4 knockout animal model. A child with 2 short alleles may have received a higher “effective” prenatal “serotonin dose” during fetal brain development, secondary to reduced serotonin transporter, thereby increasing risk of anxiety or depression symptoms during early childhood. In contrast, increased externalizing and aggressive behaviors were predicted by third-trimester maternal mood in children with 2 copies of the long allele, presumably reflecting the effect of relatively “increased” serotonin reuptake, leading to a “deficiency” in intrasynaptic serotonin, coupled with late gestational maternal anxious and depressed mood. This could be analogous to the low central serotonergic tone coupled with genetic and early rearing experiences (parental deprivation) that have been reported in nonhuman primates with impaired impulse control, aggression, and low social dominance. Similarly, early central serotonin alterations secondary to SSRI-related serotonin reuptake blockade could, via a variety of genetic and neurotransmitter-related mechanisms, lead to sustained developmental and behavioral consequences. Although the effects of prenatal SSRI exposure, which presumably also affected intrasynaptic serotonin levels in the developing brain, were not modified by SLC6A4 genotype, a direct prenatal effect of SSRIs on 5-HTT function as an influence on central serotonergic tone could not be ruled out, as has been reported in animal models.

Beyond infancy, few studies report a main effect of SSRIs. Most such studies report that irrespective of prenatal exposure, maternal mood predicts childhood behavior. In SSRI-exposed infants aged 6 to 40 months, poorer psychomotor development (Psychomotor Developmental Index and Bayley Scales of Infant Development) was observed, although the contribution of postnatal maternal mood was unclear. Early gestational fluoxetine exposure did not affect IQ, language, or behavioral outcomes in preschool-aged children compared with children with other antidepressant (tricyclic antidepressant) exposure, although development was affected by longer or more frequent episodes of postnatal maternal depression. At age 4 years, internalizing and externalizing behaviors were predicted by current levels of maternal mood in prenatally exposed children; however, externalizing behaviors and reduced task persistence and increased aggressiveness were associated with increased cord drug levels and a history of neonatal withdrawal symptoms, suggesting that early neurobehavioral and pharmacologic factors may predict subsequent behavioral vulnerability.

Several limitations need mentioning. Measures of child behavior in this study were limited to maternal reports, which raises a key concern that child behavioral ratings may have been subject to reporter bias. Anxious and depressed mothers may have been more likely to either overreport or underreport behavioral disturbances. However, if such a bias existed, as has been previously observed, this would not explain the moderating effect of the SLC6A4 genotype. This study examined associations between antenatal exposure to SSRIs and maternal mood disturbances and, in this sense, was unable to address causality or direction of effect. The study cohort was a convenience sample, and several key unmeasured maternal characteristics may have affected child outcomes, such as social and family factors inherent to mental illness during and after pregnancy. Because the mothers in the SSRI-treated group were already symptomatic and taking SSRIs at the time of conception, there may have been factors that affected fetal development long before the mothers were recruited into this study or even before they conceived. Ideally, the use of a randomized controlled study design may be regarded as an appropriate study design; however, given the evanescent nature of perinatal maternal mood disorders, a randomized study examining the effects of prenatal antidepressant exposure was not considered appropriate for ethical, logistic, and medical reasons. Although differences between children lost to follow-up from the original cohort and those studied were nonsignificant, missing data may have introduced another limitation to the generalizability of these findings. Because we had no previous behavioral data, we did not impute the missing data.

In summary, prenatal exposure to both maternal mood and SSRI antidepressants were associated with in-
creased internalizing behaviors during early childhood, whereas current maternal mood increased risk for externalizing behaviors. The impact of third trimester maternal anxiety on child mood was moderated by the child SLC6A4 genotype. In offspring with reduced 5-HTT expression (short alleles), maternal internalizing predicted increased vulnerability to anxiety at 3 years, whereas 2 long alleles predicted aggressive behaviors, suggesting fetal genotype-specific serotoninergic programming. Even with prenatal maternal SSRI treatment, mothers continue to be symptomatic, and child behavior at 3 years of age continues to be at risk.

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Correspondence: Tim F. Oberlander, MD, FRCP, Early Human Experience Unit, Developmental Neurosciences and Child Health, Child and Family Research Institute, 4480 Oak St, Room L408, Vancouver, BC V6H 3V4, Canada.

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Oberlander and Grunau. Acquisition of data: Oberlander, Brain, and Misri. Analysis and interpretation of data: Oberlander, Papsdorf, Ross, and Grunau. Drafting of the manuscript: Oberlander and Papsdorf. Critical revision of the manuscript for important intellectual content: Oberlander, Papsdorf, Brain, Misri, Ross, and Grunau. Statistical analysis: Oberlander and Papsdorf. Obtained funding: Oberlander. Administrative, technical, and material support: Oberlander, Brain, Misri, and Ross. Study supervision: Oberlander.

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REFERENCES


