Front Cell Neurosci. 2013 Oct 11;7:180. doi: 10.3389/fncel.2013.00180. eCollection 2013.

Prenatal serotonin reuptake inhibitor (SRI) antidepressant exposure and serotonin transporter promoter genotype (SLC6A4) influence executive functions at 6 years of age.

Weikum WM[1], Brain U, Chau CM, Grunau RE, Boyce WT, Diamond A, Oberlander TF.

Author information

- [1]Pediatrics, Child and Family Research Institute, University of British Columbia Vancouver, BC, Canada.

Abstract

Prenatal exposure to serotonin reuptake inhibitor (SRI) antidepressants and maternal depression may affect prefrontal cognitive skills (executive functions; EFs) including self-control, working memory and cognitive flexibility. We examined long-term effects of prenatal SRI exposure on EFs to determine whether effects are moderated by maternal mood and/or genetic variations in SLC6A4 (a gene that codes for the serotonin transporter [5-HTT] central to the regulation of synaptic serotonin levels and behavior). Children who were exposed to SRIs prenatally (SRI-exposed N = 26) and non-exposed (N = 38) were studied at age 6 years (M = 6.3; SD = 0.5) using the Hearts & Flowers task (H&F) to assess EFs. Maternal mood was measured during pregnancy (3rd trimester) and when the child was age 6 years (Hamilton Depression Scale). Parent reports of child behavior were also obtained (MacArthur Health & Behavior Questionnaire). Parents of prenatally SRI-exposed children reported fewer child externalizing and inattentive (ADHD) behaviors. Generalized estimate equation modeling showed a significant 3-way interaction between prenatal SRI exposure, SLC6A4 variant, and maternal mood at the 6-year time-point on H&F accuracy. For prenatally SRI-exposed children, regardless of maternal mood, the H&F accuracy of children with reduced 5HTT expression (a short [S] allele) remained stable. Even with increasing maternal depressive symptoms (though all below clinical threshold), EFs of children with at least one short allele were comparable to children with the same genotype whose mothers reported few if any depressive symptoms-in this sense they showed resilience. Children with two long (L) alleles were more sensitive to context. When their mothers had few depressive symptoms, LL children showed extremely good EF performance-better than any other group. When their mothers reported more depressive symptoms, LL children's EF performance was worse than that of any other group. In the face of a mother with a more depressed mood, EFs were best preserved in children prenatally exposed to SRIs and with at least one short SLC6A4 allele. Yet, prenatally-exposed LL children hold out promise of possibly superior EF if their mother's mood remains euthymic or improves.

KEYWORDS:

SLC6A4 genotype; SRI; childhood; depression; executive function; prenatal exposure; serotonin