

Neonatal Antidepressant Exposure has Lasting Effects on Behavior and Serotonin Circuitry.

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A significant fraction of infants born to mothers taking selective serotonin reuptake inhibitors (SSRIs) during late pregnancy display clear signs of antidepressant withdrawal indicating that these drugs can penetrate fetal brain in utero at biologically significant levels. Previous studies in rodents have demonstrated that early exposure to some antidepressants can result in persistent abnormalities in adult behavior and indices of monoaminergic activity. Here, we show that chronic neonatal (postnatal days 8-21) exposure to citalopram (5 mg/kg, twice daily, s.c.), a potent and highly selective SSRI, results in profound reductions in both the rate-limiting serotonin synthetic enzyme (tryptophan hydroxylase) in dorsal raphe and in serotonin transporter expression in cortex that persist into adulthood. Furthermore, neonatal exposure to citalopram produces selective changes in behavior in adult rats including increased locomotor activity and decreased sexual behavior similar to that previously reported for antidepressants that are nonselective monoamine transport inhibitors. These data indicate that the previously reported neurobehavioral effects of antidepressants are a consequence of their effects on the serotonin transporter. Moreover, these data argue that exposure to SSRIs at an early age can disrupt the normal maturation of the serotonin system and alter serotonin-dependent neuronal processes. It is not known whether this effect of SSRIs is paralleled in humans; however, these data suggest that in utero, exposure to SSRIs may have unforeseen long-term neurobehavioral consequences. *Neuropsychopharmacology* advance online publication, 13 July 2005; doi:10.1038/sj.npp.1300823.

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