

Critical Prenatal and Postnatal Periods for Persistent Effects of Dexamethasone on Serotonergic and Dopaminergic Systems

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Glucocorticoid administration to preterm infants is associated with neurodevelopmental disorders. We treated developing rats with dexamethasone (Dex) at 0.05, 0.2, or 0.8 mg/kg, doses below or spanning the range in clinical use, testing the effects of administration during three different stages: gestational days 17–19, postnatal days 1–3 or postnatal days 7–9. In adulthood, we assessed the impact on synaptic biomarkers for serotonin (5-hydroxytryptamine (5HT)) systems. Across all three regimens, Dex administration evoked upregulation of cerebrocortical 5HT_{1A} and 5HT₂ receptors and the presynaptic 5HT transporter, greatest for 5HT_{1A} receptors. The effects were fully evident even at the lowest dose. In contrast, 5HT levels in the cerebral cortex and hippocampus showed disparate patterns of temporal sensitivity, with no change after gestational treatment, an increase with the early postnatal regimen, and a decrease with the later postnatal exposure. None of the changes in 5HT concentrations were offset by adaptive changes in the fractional 5HT turnover rate. Furthermore, the critical period of sensitivity seen for 5HT levels differed from that of dopamine even within the same brain region. These findings suggest that developmental exposure to Dex during the critical neurodevelopmental period corresponding to its use in preterm infants, elicits selective changes in 5HT and dopaminergic synaptic function over and above its effects on general aspects of neural cell development, below the threshold for somatic growth impairment, and even at doses below those used clinically. Accordingly, adverse neurobehavioral consequences may be inescapable in glucocorticoid therapy of preterm infants.

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