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Insulin Sensitivity and Body Composition Effects of Prenatal Opioid Exposure

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Opioid-exposed neonates are born smaller but experience rapid catch-up growth in the first few months of life. The molecular mechanisms and impact of this rapid growth are poorly understood. Adults with opioid use disorder have lower adiponectin (a fat-cell cytokine that sensitizes the body to insulin), predisposing them to cardiometabolic diseases. To examine the effect of prenatal opioids on neonatal insulin sensitivity we analyzed the expression of salivary adiponectin genes (*ADIPOQ, ADIPOQR1*) in 20 opioid-exposed and 20 sex- and age-matched non-exposed neonates. Body composition changes (air displacement plethysmography and flank skinfold) were measured in a separate subset of 15 exposed and 11 non-exposed neonates within the first 5 days of life and by 3 months of age. Growth velocity was compared between groups. Our data showed reduced insulin sensitivity in opioid-exposed neonates, evidenced by the lower expression of *ADIPOQ* and *ADIPOR1* in this cohort than in the non-exposed cohort ($p<0.01$ and 0.06, respectively), with both sexes affected equally. Opioid-exposed neonates had lower body mass, fat-free mass, skinfold, and length measurements at birth ($p<0.05$). By 3 months of age, body composition measurements and growth velocity did not differ between the groups, with a trend towards faster skinfold changes in opioid-exposed neonates compared to controls. Prenatal opioid exposure may impact developmental programming through a reduction in insulin sensitivity since birth and changes in body composition measurements over time that resemble rapid catch-up growth. Linking genetics with body composition and anthropometric measurements is critical in understanding the metabolic effects of prenatal opioid exposure.