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The gut microbiome and insulin resistance in children born preterm

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Background: There is increasing evidence that the gut microbiome influences the development of obesity and type 2 diabetes. Studies also show that preterm children are at increased risk for insulin resistance, obesity, and cardiovascular disease. We hypothesized that adverse early life events in preterm infants may lead to alterations in the gut microbiome, which negatively affect metabolism later in life.
Aim: To examine the association between metabolic phenotype with the gut microbiome composition and functional capacity in healthy prepubertal children born very preterm (<32 weeks of gestation; n=51) compared to those born at term (37–41 weeks; n=50).
Results: Participants were healthy prepubertal children aged 5 to 10 years born very preterm (<32 weeks of gestation; n=51) and at term (37–41 weeks; n=50). Children born very preterm were younger (7.8±1.4 vs 8.3±1.4 years; p=0.034) than peers born at term. No difference were observed in sex ratio (p=0.90) between the two groups. Preterm children were shorter (height SDS 0.31 vs 0.92; p=0.0006) and leaner (BMI SDS -0.20 vs 0.29; p<0.0001) than those born at term. Importantly, after adjustment for adiposity and other confounders, children born very preterm had lower insulin sensitivity than term controls (9.2 vs 12.5 $x10^{-4}\cdot min^{-1}$(mU/l); p=0.0007). Stool metatranscriptomics identified *Collinsella* species as being significantly associated with children who were born preterm (highly significant with LDA score >4.0, LefSe). There were also functional changes in the activity of the microbiome in children born preterm, including glutamate and arginine metabolism, known to be involved in glucose homeostasis. Changes to the metabolites within the preterm fecal and plasma correlated with the observed phenotypes.
Conclusion: Children born very preterm have reduced insulin sensitivity and display differences in gut microbiome species and activity. We speculate that (i) these changes in the gut microbiome of children born preterm were established in early infancy, and (ii) the altered gut microbiome contributes to insulin resistance.