



A detailed analysis of the gut microbial diversity and metabolic activity in children with obesity of different aetiology and lean controls

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It is not yet clear whether differences between lean and obese people are a cause of obesity or if it is an effect of different dietary patterns between lean and obese individuals. We explored the possibility of reverse causality by comparing gut microbial composition and bacterial metabolic activity in children with obesity of different aetiology.

Faecal samples were collected from children/young adults with “simple” obesity ($n = 17$), hypothalamic obese ($n = 12$ with Prader-Willi syndrome), hypothalamic lean ($n = 10$ with Prader-Willi) and healthy lean controls ($n = 20$). Faecal short chain fatty acids (SCFA), sulphide and ammonia were measured. The fermentative capacity of the gut microbiota from each subject group was assessed with 24 h *in-vitro* batch culture fermentations using 5 different carbohydrates (apple pectin, raw potato starch, wheat bran, raftilose and maize starch). The V4 region of the 16S rRNA gene was sequenced on the MiSeq platform to explore differences in bacterial community taxonomy between groups.

Faecal SCFA concentration did not differ between children with obesity of different aetiology. Obese (“simple” & hypothalamic together) children had significantly higher concentration of propionate than lean (control & lean hypothalamic together) children ($72.7 \mu\text{mol/g}$ dried faecal material vs. $51.1 \mu\text{mol/g}$, $p = 0.008$). Total SCFA concentration was positively correlated with BMI z-score (Spearman correlation = 0.21 , $p = 0.03$). No significant differences were observed in the 24 h fermentation studies.

There was a significant relationship (p -value = 0.023) between group and rarefied OTU richness with a higher diversity observed in both lean compared with obese groups. There was a highly significant effect of obesity on community structure and a mild impact of pathology explaining 5% of total variance. A higher frequency of *Dorea* and *Collinsella* and a lower frequency of *Veillonella* and *Alistipes* were observed in obese children. There was a significant relationship between the OTU community composition and weight gain ($R^2 = 0.035$, $p = 0.0121$). Ten OTUs significantly correlated with weight gain.

These results do not support the role of the gut microbiota in the aetiology of obesity but provide strong evidence to suggest that the findings reported in this and previous studies are the result of obesity and likely to be due to different dietary patterns and intake between lean and obese children.

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