Intestinal microbiota development differs between pubertal girls and boys

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Introduction

Adolescence is one of the turning points in the human microbiota composition (1), but it is unknown, whether the microbial transformation is connected to sexual maturation. In mice, the change in the composition of microbiota during puberty is sex-specific and associated with changes in testosterone levels (2). The development of microbiota in early childhood is better understood compared to the pubertal period (3). The aim of the current work was to investigate the association between intestinal microbiota and pubertal timing.

Subjects and methods

The study was implemented on allergy-prevention-trial cohort including 1018 participants with high risk for allergy (4). The subjects randomly received a mixture of four probiotics and a prebiotic or placebo. The treatment was started perinatally for the participants mothers at the end of their pregnancy and was continued directly to the participants for the first six months of their life. The treatment had no effect on growth.

At 13 years of follow up, 415 participants provided a fecal sample, and their growth data was collected from the school health service records for analysis (5). Height progression was modelled with a polynomial function and individual growth velocity curve was produced for each participant.

We determined the *age at peak height velocity* (APHV) using the derivative of the growth velocity curve and used it as a marker for timing of puberty. Another marker for pubertal maturation, *time from peak height velocity* (TPHV), was calculated by subtracting the age at fecal sampling from the APHV. The analysis was limited to genus-level and correlations with $p<0.001$ are reported.

Microbiota composition of the samples was analyzed by 16S rRNA amplicon sequencing on a Illumina platform, which has been previously described (6). Samples with less than 900 reads were excluded. The statistical analysis was carried out with R using mare-package, which relies on USEARCH. The analysis was adjusted for relevant confounders.

Results

Sufficient growth data for the assessment of puberty timing was available in 35% (n=145) of the 415 participants (60% females, 40% males). One girl and 16 boys were prepubertal based on self-reported Tanner staging. The genera with statistically significant ($p<0.001$) positive or negative correlations with TPHV are presented in the table.

Results for APHV were very similar to those with TPHV.

Conclusion

Our results, for the first time, show that the timing of human puberty is correlated with fecal microbiome in a sex-specific manner, suggesting the impact of sex hormones in the microbiota development. For further confirmation, the analysis has to be repeated in different study populations.

The genera correlating with TPHV ($p<0.001$)

Boys

Genera	β
With zero-observations	
Burkholderia	-1.549
No zero-observations	
Actinomyces	-1.091

Girls

Genera	β
With zero-observations	
Gemella	0.573
Barnesiella	-0.145
Oscillospira	-0.493
No zero-observations	
Anaerospora	0.350
Solobacterium	0.337
Megamonas	-1.789

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Background picture (*Bacillus subtilis*) by Y Tambe (Wikimedia Commons)