Gut Microbiome of North-American Children with and without Prader-Willi Syndrome (PWS)

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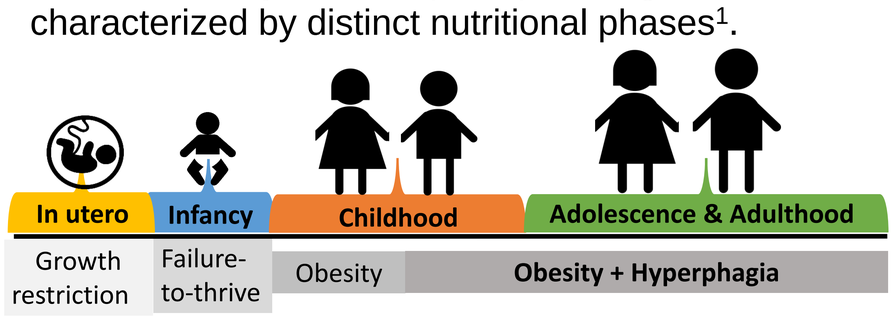
INTRODUCTION

- Prader-Willi Syndrome (PWS) is a genetic disorder characterized by distinct nutritional phases[1].



- The pathogenesis of hyperphagia and weight gain in PWS is poorly understood[2].
- Evidence suggests an etiological contribution of dysbiotic gut microbiota in the metabolic derangements of obesity[3].

AIM & METHODS

This study aims to characterize the gut bacterial and fungal composition of children with and without PWS (ages 3-17 years)

Cross-sectional study design

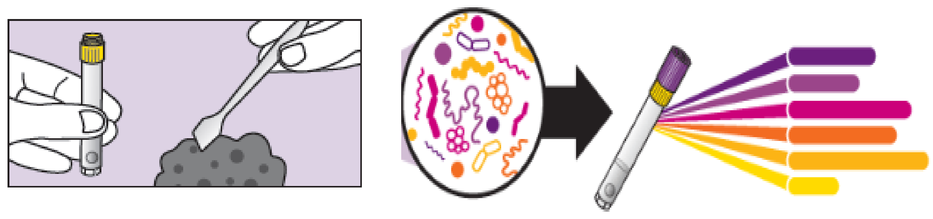
A stool sample, 3-day dietary record, hyperphagia questionnaire[2], and anthropometric measures (height, weight, waist-circumference) were collected.

METHODS (cont.)

Participants

Children with **PWS** were recruited from the PWS clinics at U of Alberta and remotely (Foundation for Prader-Willi Research Canada/USA & USA-PWS association). Age and BMI-matched **controls** were recruited from advertisements through the U of Alberta bulletin boards and mail distribution lists.

Stool sample collection



OMNIgene® GUT OMR-200 (DNA Genotek)

Statistical analysis

- Composition of the bacterial and fungal community by 16S rRNA and ITS gene amplicon sequencing
- Operational taxonomic units (OTUs), by Mothur
- Differences in α- and β-diversity indices (α: Shannon, Simpson, Chao1; β: Jaccard, Bray-Curtis) and differential abundance testing (DESeq2, R-package) were assessed between PWS and control groups.
- Relationship of PWS-status (with or without PWS) and weight status (normal-weight vs. overweight) to OTU-level profiles (bacterial & fungal) using canonical correspondence analysis.

RESULTS

Table 1. Participants characteristics

Variable	PWS (n=25)	Control (n=25)	P-values
Sex (F/M)	14/11	9/16	0.162
Age (Years)	6.2 (5.2, 12.9)	8.8 (6.4, 10.5)	0.8
BMI z-score	0.8 (0.4, 1.6)	0.73 (0.02, 1.4)	0.588
Weight Status (OWOB/NW)	10/15	8/17	0.565
Hyperphagia scores**	19 (16, 26)	15 (14, 18)	**0.005***
Energy intake (Kcal)§	1865.8 (1175.7, 1499.8)	1911.5 (1540.4, 2064.4)	**0.000***
Protein (g)	66.3 (65.2, 76.3)	64.4 (55.5, 73.2)	0.178
Carbohydrates (g)	219.2 (148.5, 206.3)	225.3 (192.7, 240.0)	**0.005***
Fat (g)	199.3 (183.9, 210.8)	202.2 (196.1, 209.4)	0.872

Female (F); Male (M); Prader-Willi Syndrome (PWS); Body mass index (BMI); Overweight/Obese (OWOB); Normal weight (NW). Data in Median (25th and 75th percentiles). *p<0.05 with independent Student's t test. **Scores from 12 to 39 for PWS and 12 to 25 for controls (min. possible is 11/55). §Energy-adjusted intake.

Figure 1. Discriminative features in LDA. (A) Discriminative bacterial genera in PWS vs CON; **(B)** Discriminative fungal genera in PWS vs CON. Red: PWS; Light blue: CON

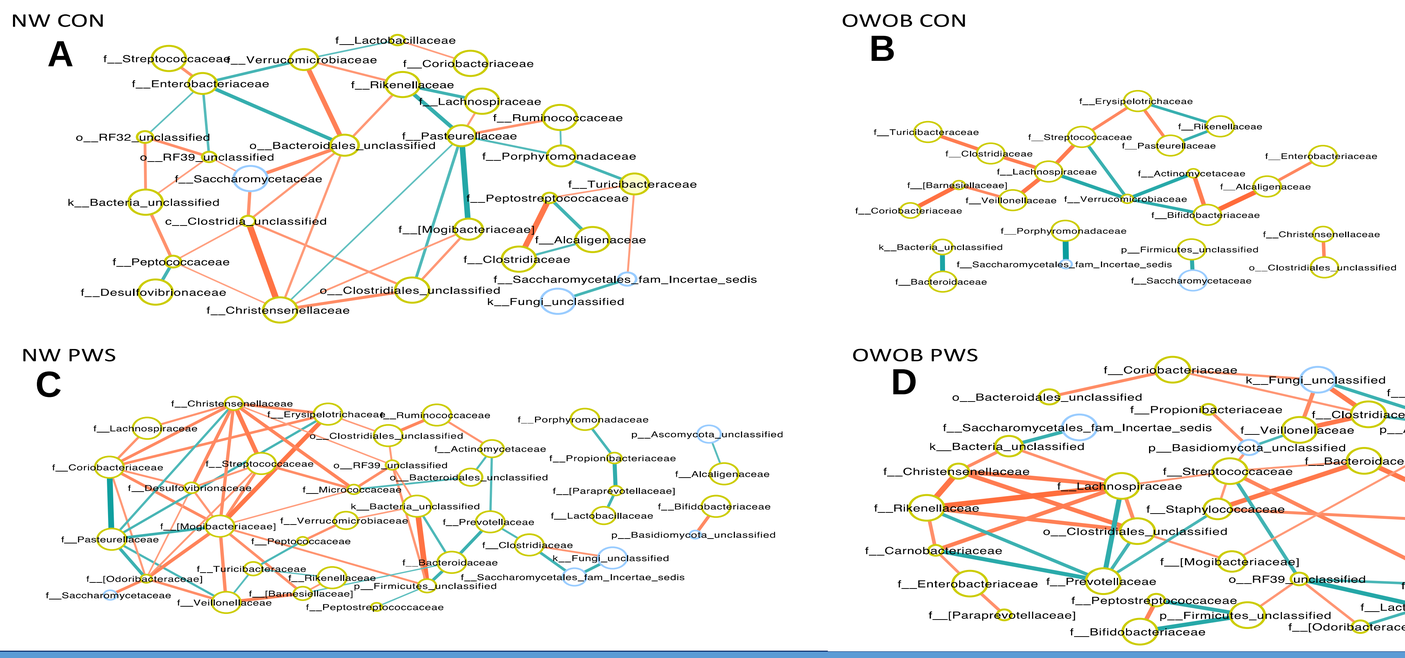


Figure 2. Microbial family co-occurrence networks for four subgroups.
(A) Normal-weight (NW) control children. **(B)** Over-weight or obese (OWOB) control children. **(C)** NW PWS children. **(D)** OWOB PWS children.

Yellow nodes: bacterial families; grey: fungal.
Green lines: negative correlations; orange: positive.
Connector line thickness: value of Spearman correlation coefficient (ρ), and family names on the nodes represent the proposed taxonomy by the Greengenes database.
Size of nodes indicates the occurrence frequency in each subgroup.

CONCLUSIONS

Differences were observed in α-& β-diversity indices between groups. Higher differential abundance of taxa associated with inflammation and obesity and lower differential abundance of taxa linked with improved metabolic outcomes were observed in PWS compared to controls. Characterization of microbiota functional differences between groups is currently ongoing.

ACKOWLEDGEMENTS

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