BRIEF COMMUNICATION:
RESEARCH REPORT

CURRENT DEVELOPMENTS IN NUTRITION

Maternal and Pediatric Nutrition

Effect of High-Protein Diet on Postprandial Energy Expenditure in Children with Prader-Willi Syndrome: A Pilot and Feasibility Study

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ABSTRACT

The aim of this study was to explore the feasibility of measuring a postprandial increase in energy expenditure (ΔEE) using a state-of-the-art whole-body calorimetry unit (WBCU) in children and youth with Prader-Willi syndrome (PWS). Five participants (aged 10–25 y) received both a standard and a high-protein diet in a random order (crossover design). Resting energy expenditure, postprandial ΔEE 6 h after intake of a standard [15% of total energy (TE)] and a high-protein (30% TE) meal, and respiratory exchange ratio (RER) were measured in a WBCU. No differences were observed in ΔEE comparing the 2 meals. Mean RER was lower following the high-protein meal (0.80 ± 0.01) compared with the standard meal (0.87 ± 0.02) ($P = 0.009$). Despite the high participant burden, it was feasible to conduct this metabolic test in children and youth with PWS. This study paves the way for further studies targeting EE in this patient population. *Curr Dev Nutr* 2021;5:nzab016.

Keywords: Prader-Willi syndrome, high-protein diet, diet-induced thermogenesis, energy metabolism, energy expenditure, whole-body calorimetry unit

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Abbreviations used: DIT, diet-induced thermogenesis; EE, energy expenditure; GH, growth hormone; PWS, Prader-Willi syndrome; REE, resting energy expenditure; RER, respiratory exchange ratio; TE, total energy; TEE, total energy expenditure; WBCU, whole-body calorimetry unit; ΔEE, increase in energy expenditure.

Introduction

Prader-Willi syndrome (PWS) is a rare genetic disorder characterized by hyperphagia and progressive obesity (1). The significant weight gain that leads to obesity in children with PWS is thought to be caused, in part, by a chronic imbalance between energy intake (EI) and energy expenditure (EE) (2, 3). It has been suggested that individuals with PWS may present a reduced diet-induced thermogenesis (DIT) secondary to hormonal dysregulation, such as growth hormone (GH), thyroid hormone, and testosterone deficiencies, which may lead to a reduced overall EE due to their effects on fat-free mass (4).

DIT is the energy expended through digestion, absorption, and storage of nutrients and contributes to ∼10–15% of an individual's total energy expenditure (TEE) (5). The postprandial increment of EE (ΔEE) is considered a surrogate measure of DIT (6).

Meals of similar energy content but with different macronutrient composition may impact an individual's DIT (7). Meals high in protein have been shown to promote weight loss and maintenance through appetite control and food-intake regulation (8–10). Additionally, a high-protein intake has been associated with a 50% increase in fat oxidation (11), which could lead to a reduction in body fat. In the adult population, studies reported that increased protein intake in the context of an energy-balanced meal produced a prolonged DIT, which, in turn, contributed to greater TEE (12). Increasing DIT through modifying diet composition could be a clinical strategy for individuals with PWS in order to promote weight management; however, there is a paucity of information on DIT in individuals with this condition (4). The aim of this study was to explore the feasibility of measuring postprandial ΔEE using a state-of-the-art whole-body calorimetry unit (WBCU) in children and youth with PWS.

Methods

Participant recruitment

Individuals aged 10 to 25 y with a confirmed diagnosis of PWS and free thyroxine and thyroid-stimulating hormone concentrations within the normal range were eligible to participate in this study. Exclusion criteria included the presence of any medical condition known to affect body composition (e.g., diabetes mellitus, chronic inflammatory bowel disease, chronic severe liver disease, kidney disease, neurologic disorders) and investigational drug use in the year prior to study enrollment.

TABLE 1 Study breakfast meals provided during the test days

	Meal	
	Isocaloric standard breakfast	**Isocaloric high-protein breakfast**
Protein	15% of total kcal	50% of total kcal
Fat	30% of total kcal	30% of total kcal
Carbohydrate	55% of total kcal	20% of total kcal
Foods	• Milk • Egg wrap • Orange fruit slice • White toast with strawberry jam	• Milk with whey protein • Turkey egg scramble • Tortilla whole wheat

Participants were recruited between 2016 and 2019 from the Stollery Children's Hospital pediatric endocrine clinics in Edmonton, Alberta, Canada.

The study protocol was approved by the University of Alberta's Health Research Ethics Board (Pro00066276). Written informed consent and assent were obtained from all participants and parents before participation.

Experimental design and procedure

A pilot, randomized, nonblinded crossover study was conducted over 3 study visits. Due to the nature of the meal testing, both participants and researchers were aware of the meal being tested. Each study visit was separated by a 2- to 4-wk washout period. All visits were conducted in the morning after an overnight 8-h fast.

At visit 1 (baseline), participants underwent anthropometric and resting energy expenditure (REE) assessments. Pubertal status was self-reported (by children assisted by their parents) using the Tanner stage scale (13). On test days (visits 2 and 3), anthropometrics, REE, and postprandial ΔEE were assessed.

Experimental diets.

Participants were randomly assigned to receive 2 different standardized isocaloric diets at visits 2 and 3: *1*) a high-protein diet (% of total energy: 20% carbohydrates, 50% protein, and 30% fat) and *2*) a standard diet, which represented a typical Canadian diet (14) (% of total energy: 55% carbohydrates, 15% protein, and 30% fat). Both diets included prepared meals for a full day (breakfast, lunch, dinner, and morning/afternoon snacks) and contained caloric content to meet each participant's estimated energy requirements.

One day prior to visits 2 and 3 (test days), participants were asked to visit the study site to consume breakfast, according to the diet they were assigned to. The same day, participants received 2 additional precooked and packaged meals (lunch and dinner) with 2 snacks (morning and evening snacks) to take home with them to complete a full day's intake. On each of the 2 test days, participants consumed a breakfast meal at the study site according to the diet they received the previous day (standard or high protein). Both breakfast meals provided 35% of each participant's estimated 24-h energy requirements (**Table 1**).

Anthropometry.

During all visits, weight and height were measured. The average of all visits' measurements was calculated and used to assess BMI percentiles, using Epi Info 2000 (CDC; http://www.cdc.gov/epiinfo/).

REE and postprandial increment of ΔEE assessments.

These assessments were conducted using an open-circuit WBCU (geometric volume of 28.74 m^3). In this temperature-controlled unit, gas exchanges (oxygen and carbon dioxide volumes) are calculated on a per minute basis using Advance Optima AO2000 Series CO2 analyzer (ABB Automation GmbH) and the Oxymat 6 O2 analyzer (Siemens AG). A computer collected this information via the National Instruments NI USB-6221 device (National Instruments Corporation) using the PMCSS software version 1.8 (Pennington Metabolic Chamber Software Suite; Pennington Biomedical Research Center).

Visit 1 (baseline). REE was measured for 60 min in a WBCU after fasting for ≥8 h. This REE value was considered the "fixed REE" when estimating postprandial ΔEE. This fixed REE represents the REE in a fasted state, which followed consumption of a regular diet the previous day. The first 30 min were excluded from the analysis to account for test acclimatization. Participants' REE results were used to calculate their 24-h energy requirements ("REE × activity factor") (15). A physical activity factor of 1 was used to reflect a "sedentary lifestyle" as previously documented in children with PWS (16).

Visits 2 and 3. REE and respiratory exchange ratio [RER; ratio of carbon dioxide production (VCO_2) and oxygen consumption (VO_2)] were measured in a fasted state for 1 h in the WBCU. The first 30 min of assessment were also excluded from the analysis. This REE measurement served as the baseline REE. This baseline REE represents the REE in a fasted state after a day of consuming the assigned study meal. Immediately after this measurement and without leaving the room, participants consumed the breakfast meal within 30 min. After finishing the breakfast, EE was measured for a total of 6 h. Participants were allowed two 10-min breaks at 2 and 4 h, without leaving the room.

Postprandial ΔEE associated with the standard and high-protein meal was calculated as the difference between the 6-h EE and the baseline REE measured at each corresponding test visit. It was also calculated as the difference between 6-h EE measured after each breakfast was consumed subtracted from REE measured at baseline visit (fixed REE).

Statistical analysis

Statistical analyses were performed using SPSS version 24 for Windows (IBM Corp.). A P value < 0.05 was considered statistically significant. All values were reported as means and SDs. A paired-samples t test was used to compare the mean postprandial ΔEE and RER between the 2 study meals for each participant in the study.

TABLE 2 Participants' baseline characteristics[1]

Characteristics	Values
Age, y	15 ± 3.7 (11–20)
Males/females, *n*/*n*	1/4
Height, cm	152.2 ± 11.0 (137.5–168.4)
Weight, kg	61.3 ± 18.3 (40.4–90.0)
BMI, kg/m^2	26.4 ± 7.8 (21.4–40.2)
BMI percentile	85.7 ± 10.5 (70.2–98.3)
Baseline protein intake, %TE	16.4 ± 7 (13.7–21.1)
Baseline REE, kcal	1686 ± 234 (1538–2098)

[1] $n = 5$. Values are means ± SDs (minimum–maximum ranges) unless otherwise indicated. REE, resting energy expenditure; %TE, percentage of total energy.

Results

The baseline characteristics of the study participants are shown in Table 2. Five participants (4 females and 1 male) completed both arms of the study. Participants' weight remained stable during the duration of the study (data not shown). Self-assessed pubertal status ranged from Tanner stage II to V. All participants were taking GH treatment prior to study enrollment; no changes in GH treatment were made during the course of the study. All participants reported consuming all the meals provided to them.

Mean REE measured at baseline visit (fixed REE) was 1686 ± 234 kcal. Mean REE measured at the following day after the intake of the standard diet was 1590 ± 168 kcal, and mean REE measured the following day after the intake of the high-protein diet was 1651 ± 188 kcal.

No differences were detected in mean postprandial ΔEE (calculated using the baseline REE) between the standard meal and high-protein meal (184 ± 148 vs. 200 ± 188 kcal, respectively; $P = 0.74$). Likewise, mean postprandial ΔEE calculated using the fixed REE was not different for the standard meal compared with the high-protein meal (89 ± 149 vs. 165 ± 146 kcal, respectively; $P = 0.20$). Mean RER was lower following the high-protein meal (0.80 ± 0.01) as compared with the standard meal (0.87 ± 0.02) ($P = 0.009$).

Discussion

The impact of dietary macronutrient content on postprandial ΔEE in children and youth with PWS is poorly understood. Although of limited sample size, this is the first study that has assessed postprandial ΔEE in children and youth with PWS using the state-of-the art technique of WBCU. One previous study (16) examined TEE and REE using a WBCU in children and youth with PWS. However, our study is the first to determine postprandial ΔEE using this technique, showing that, despite the high participant burden required, it is feasible to conduct this metabolic test in children and youth with PWS.

Although no differences in postprandial ΔEE were observed in this pilot study including 5 participants, our data showed that RER was lower after the consumption of a high-protein meal compared with the standard meal, suggesting a shift towards fat rather than carbohydrate as a fuel source. These findings need to be confirmed in larger controlled studies; however, they provide insight into the feasibility of conducting this form of assessment in patients with PWS and the potential of a high-protein diet to modify RER in these patients. RER is affected by the availability of dietary and stored macronutrients, increasing with the intake of a high-carbohydrate meal and decreasing during fasting or after a high-fat meal intake. A previous study found no differences in RER between 11 adults with PWS and 12 BMI-matched individuals with healthy weight in response to a standardized breakfast of mixed high-carbohydrate and high-fat content (600 kcal, 50% carbohydrate, 35% fat, 15% protein) (17). However, the adaptation to adjust fuel oxidation to fuel availability occurs between 1 and 7 d (18); this may help explain the difference in our findings. In this previous study, RER was measured the same day after consuming the breakfast, while in our study RER was measured after 1 d of consuming the corresponding study meal.

REE measured in a fasted state is affected by the prior day's diet (19–21); thus, to minimize any potential effects, the REE measured at the baseline visit (fixed REE) was also used to calculate postprandial ΔEE in our study. Results showed that postprandial ΔEE, calculated with fixed REE, was double after the high-protein meal intake as compared with the standard meal intake; however, this difference was not statistically significant within our limited study sample size.

Only 1 study has investigated DIT in individuals with PWS compared with BMI-matched and healthy-weight individuals (17). The authors found no difference in DIT between groups after the consumption of a meal of moderate protein content (600 kcal, 15% protein).

Further studies with larger sample sizes and a proper control group are required to compare the effects of meals with low protein–high carbohydrate and standard-fat, standard/typical intake, and high protein–low carbohydrate and standard fat on DIT in children with PWS, considering factors that influence response to energy metabolism (e.g., pubertal status, body composition, and sex). This pilot study provides valuable information on the feasibility of measuring ΔEE in children and youth with PWS in such a state-of-the-art technique. Also, it is the first step in understanding the metabolic implications of a high-protein diet in children and youth with PWS as a therapeutic option to improve overall energy balance and weight maintenance. Finally, it provides initial data to make a power calculation for a larger study.

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