fMRI Studies of Food Motivation in Prader-Willi Syndrome

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ABSTRACT

Prader-Willi syndrome (PWS) is a complex genetic disorder associated with chromosome 15 abnormalities, hyperphagia and obesity. As such, it may provide a genetic model for overeating and obesity in otherwise healthy individuals. We have completed an initial study using fMRI to evaluate neural responses to images of food in individuals with PWS and age-matched healthy-weight individuals (HW) before and after eating a 500-calorie meal. We predicted that specific brain areas responding to food images would differ between individuals with PWS and HW controls according to state of motivation (pre-meal vs. post-meal). Data are reported for eight subjects with PWS and eight age-matched healthy-weight individuals who underwent fMRI scanning. The PWS group exhibited greater activation than the HW group in the bilateral MPFC, OFC, and amygdala after eating. Our findings suggest that individuals with PWS display enhanced activation in limbic and paralimbic regions ***after eating***. These initial findings highlight neural networks underlying satiation failures in PWS. We are now in the process of recruiting an additional 15 PWS participants into the study so that we can separately examine fMRI data in the three most common genetic subtypes: Uniparental Maternal Disomy 15 (UPD), Deletion Type I, Deletion Type II.

INTRODUCTION

Prader-Willi syndrome (PWS), a classical disorder due to genomic imprinting, is caused by abnormalities of chromosome 15 and associated with hyperphagia and obesity. PWS consists of three genetic subtypes (paternal chromosome 15q11-q13 deletion- in 70% of cases; uniparental maternal disomy 15 (UPD)- both 15s from the mother in 25%; and imprinting defects in 3%. Recently, the typical 15q11-q13 deletion has been classified into Type I (longer) or Type II (shorter) deletions and behavioral differences have been observed between the two deletion types. Although it is probable that hyperphagia in PWS results in part from neural dysfunction, few studies have investigated the link between brain activity and food motivation in this population.

The purpose of the current study is to expand our PWS cohort to include adequate numbers from each of the three most common genetic subtypes: UPD, Deletion Type I, and Deletion Type II. Results from this study should provide important information concerning differences between subtypes of PWS, and ultimately important clues regarding genetic contributions to hyperphagia and obesity, possibly leading to new treatment modalities. This poster illustrates the Methods and Results of our initial study as well as Summary, Conclusions, and Future Directions.

METHODS

PARTICIPANTS

- n = 8 individuals with PWS
  - Mean age = 15.4 years
  - Mean BMI = 30.9*
- n = 8 healthy weight individuals
  - Mean age = 14.9 years
  - Mean BMI = 19.1*

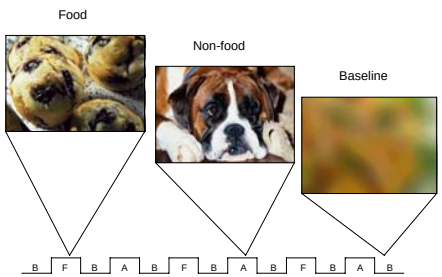
* Statistically different between groups

PROCEDURE

- Pre-Meal/Post-Meal Group (n = 4)
  - Scanned first when hungry (Session 1)
  - Scanned again immediately after eating (Session 2)
- Post-Meal/Pre-Meal Group (n = 4)
  - Scanned first immediately after eating (Session 1)
  - Scanned again when hungry (Session 2)
- Time between meals: 4 hours
- Standardized meal: ~ 500 calories

IMAGING PARAMETERS AND STIMULI

- Siemens 3T Magnetom Allegra system
- Anatomic SPGR scan
- Two functional EPI scans in 43 contiguous coronal slices (TR/TE = 3000/40 ms)
- Total scanning duration/session = 25-30 minutes
- Block design: 10 images per block (presentation time = 2.5 seconds; ISI = 0.5 seconds)

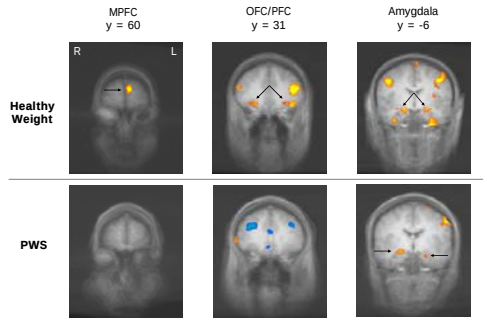


DATA PROCESSING AND ANALYSIS

- Functional data preprocessing using BrainVoyager 2000
- Data for each subject/group concatenated
- Two levels of comparison, based on t-tests between voxels in a priori regions of interest:
  - Within-group: Food vs. Baseline in Pre-Meal & Post-Meal states
  - Group (PWS vs. HW) x Condition (Pre-Meal vs. Post-Meal) Interaction
  - Threshold level p<.01, corrected for multiple comparisons across whole brain

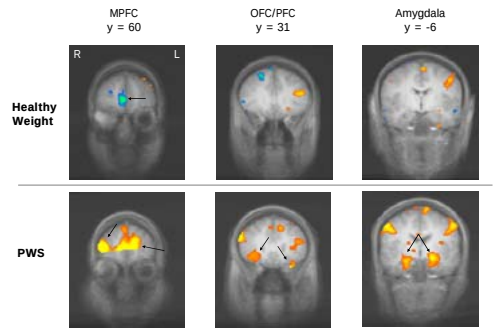
RESULTS: PRE-MEAL

- HW Group: Increases to food in MPFC, OFC, amygdala, insula, anterior cingulate cortex (ACC), parahippocampal gyrus, and fusiform gyrus
- PWS Group: Increases to food in amygdala and hippocampus; decreases to food in lateral PFC (LPFC)



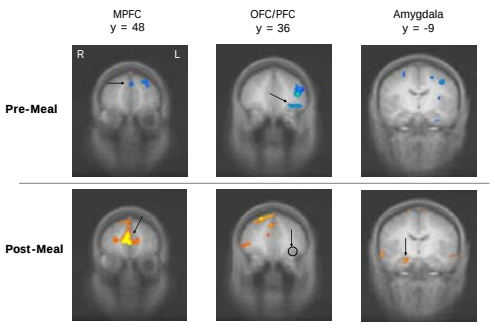
RESULTS: POST-MEAL

- HW Group: Decreases to food in MPFC and increases to food in LPFC and insula
- PWS Group: Increases to food in MPFC, LPFC, OFC, amygdala, insula, parahippocampal gyrus, and fusiform gyrus



BETWEEN GROUP INTERACTION

- Pre-Meal: HW > PWS in MPFC, OFC, ACC, insula, parahippocampal gyrus, and fusiform gyrus
- Post-Meal: PWS > HW in MPFC, OFC, amygdala, insula, ACC, hippocampal formation, and fusiform gyrus



SUMMARY, CONCLUSIONS, AND FUTURE DIRECTIONS

- Results indicate hyperfunction in limbic and paralimbic cortical regions in PWS ***after eating***.
- In contrast to HW individuals, PWS participants fail to show normalization in these regions after eating. Instead, they demonstrate dramatic increases. Thus, satiation failures in PWS appear to have a neural basis and findings support the use of PWS as a *model of extreme overeating and obesity*.
- With funding from the Heartland Genetics Collaborative, we are recruiting an additional 15 PWS participants so that we can examine differences in brain function in the three most common genetic subtypes seen in this syndrome.