Weight status and eating behavior affect how the brain regulates food craving

Anja Dietrich[1], Maurice Hollmann[1], David Mathar[1,2], Arno Villringer[1,2,3,4,5], and Annette Horstmann[1,2,6]

[1]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig; [2] IFB Adiposity Diseases, Leipzig University Medical Center;
[3]Clinic for Cognitive Neurology, University Hospital Leipzig; [4]Mind and Brain Institute, Berlin School of Mind and Brain, Humboldt-University and Charité;
[5]Leipzig University Medical Center, SFB 1052A1, Leipzig, Germany; [6]Leipzig University Medical Center, SFB 1052A5, Leipzig, Germany

Introduction

Food craving is a driving force for overeating and obesity. Consequently, therapeutic approaches targeting craving are promising tools to successfully control weight.[1] To improve such treatments it is **necessary to understand the underlying brain mechanisms of food craving regulation**. However, relationships between these brain mechanisms and weight status are still open issues. Previous findings are inconsistent in that, e.g., no,[2,3] smaller, [4,5,6] or larger[7,8] responses in executive control areas of the lPFC have been reported in response to appetizing food pictures with higher BMI. Reasons for this lack of knowledge might be gaps in the studied body mass index (BMI) distribution and a focus on potential linear associations with BMI. Quadratic relationships – as demonstrated between BMI and behavior (reward sensitivity[9] and eating-related self-control[10]) have not been studied. We investigated brain mechanisms of craving regulation with the help of functional magnetic resonance imaging (fMRI) in a balanced sample including normal-weight, overweight and obese participants. **Associations between characteristics of obesity, eating behavior** (*Three-Factor Eating Questionnaire*, TFEQ; scales: *Cognitive Restraint*, CR; *Disinhibition*, DIS)[11] **and brain function** were investigated, **focusing on quadratic relationships.**

Methods

subjects and paradigm:

- study is an extension to Hollmann et al. (2012) [3]
- 43 hungry female participants (age: 21 - 36 years, mean: 26.7 +/- 3.5; BMI: 19.4 - 38.8 kg/m², mean 27.5 +/- 5.3 SD; CR: 0 - 15, mean 7.0 +/- 4.0 SD; DIS: 1 - 14, mean 7.49 +/- 3.6 SD)
- presented with 60 high-caloric food images individually pre-rated according to tastiness and healthiness
- instruction: admit to the upcoming craving for the food stimuli or regulate it using every-day strategies (Figure 1)

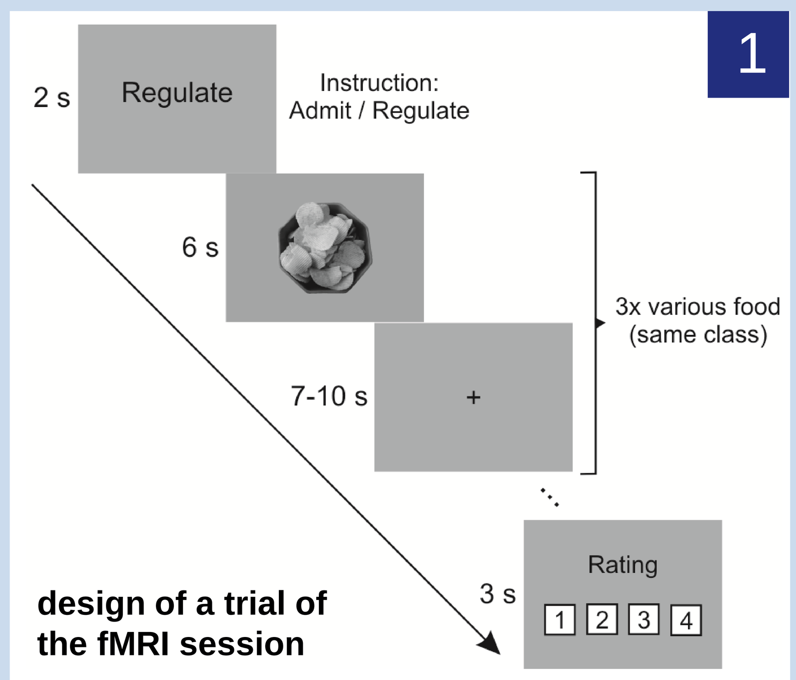

Figure 1: The instruction "Admit" or "Regulate" referred to the three following food items. According to individual pre-ratings pictures of one trial belonged either to the class "tasty" or "not tasty". After each trial, participants rated their performance on a scale of 1-4 via button-press inside the MR scanner.

MR data acquisition: Siemens 3T TIM Trio whole-body MRI scanner
EPI sequence: TR = 2 s, TE = 27 ms, flip angle = 90°, matrix size = 64 x 64 voxel, voxel size = 3.0 x 3.0 x 3.6 mm3, AC/ PC aligned

data analysis (BOLD response): based on SPM 8 and Matlab 2010b

first level analysis: general linear model; regressors: REGULATE_TASTY, REGULATE_NOT_TASTY, CRAVE_TASTY, CRAVE_NOT_TASTY

second level analysis: estimates of the regulation contrasts were regressed on BMI, BMI², CR, and DIS (age and/ or BMI as regressor(s) of no interest)

functional connectivity analysis: (psychophysiological interaction, PPI)[12]

- source regions (spheres, r=4mm): putamen: -33, -9, -3; amygdala: -30, -3, -18; insula: -39, -12, 9 (BOLD activity related to BMI)
- PPI terms were regressed on BMI, BMI², CR, and DIS

Results

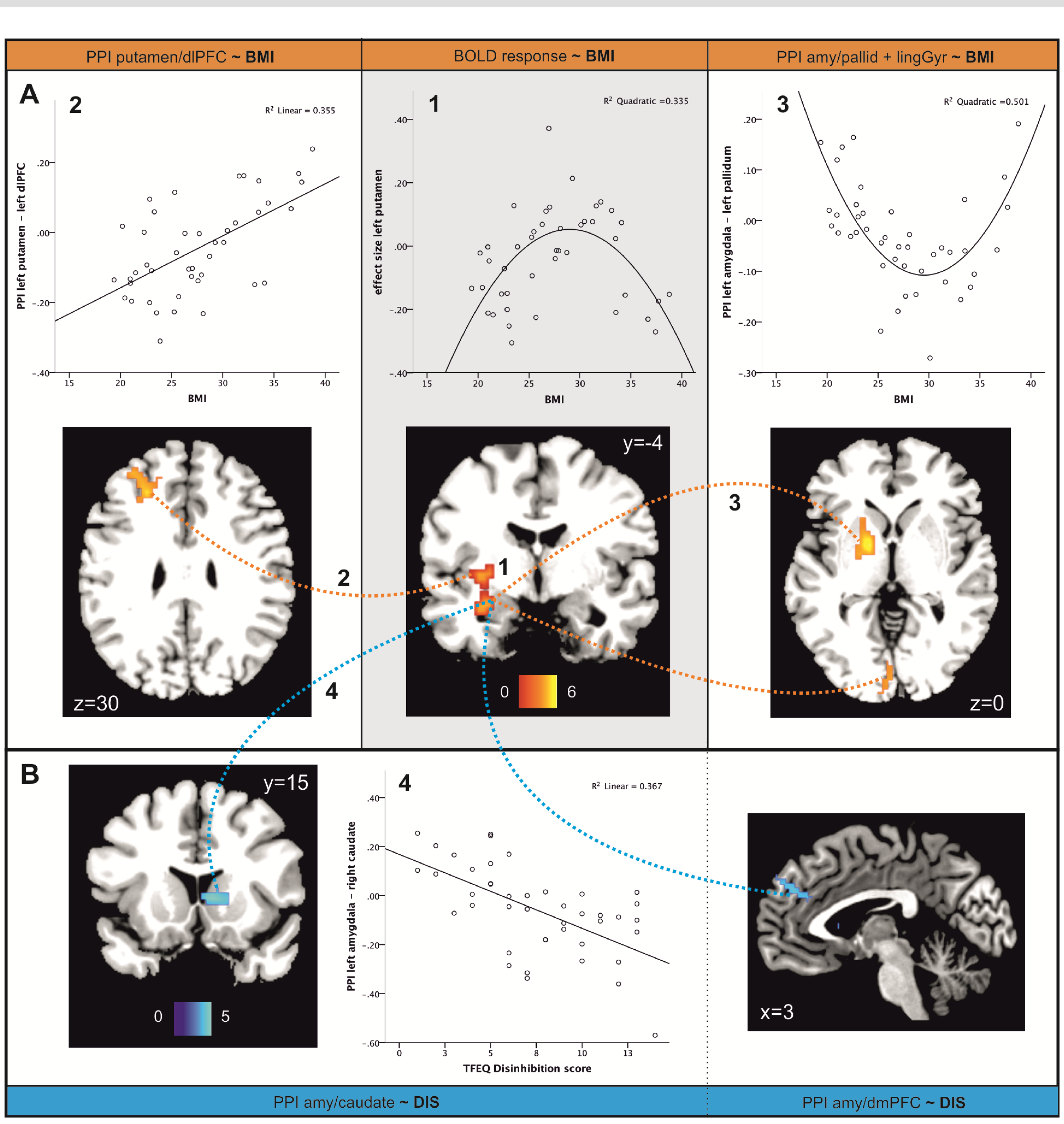

Figure 2:
Neural correlates of volitional food craving regulation (REGULATE_TASTY > CRAVE_TASTY): Modulation by BMI and *TFEQ Disinhibition*.

(A - left)
Functional connectivity between putamen and dorsolateral prefrontal cortex (dlPFC) linearly scaled with BMI (2).

(A - center)
During regulation, BMI correlated with brain activity in left putamen, amygdala, and insula in an inverted U-shaped manner (1, insula not depicted).

(A - right)
Functional connectivity of amygdala with pallidum (pallid, 3) and visual cortex (lingual gyrus, lingGyr) was non-linearly (quadratic) associated with BMI.

(B)
TFEQ Disinhibition scaled negatively with the strength of functional connectivity between amygdala and dorsomedial prefrontal (dmPFC) cortex as well as caudate (4).

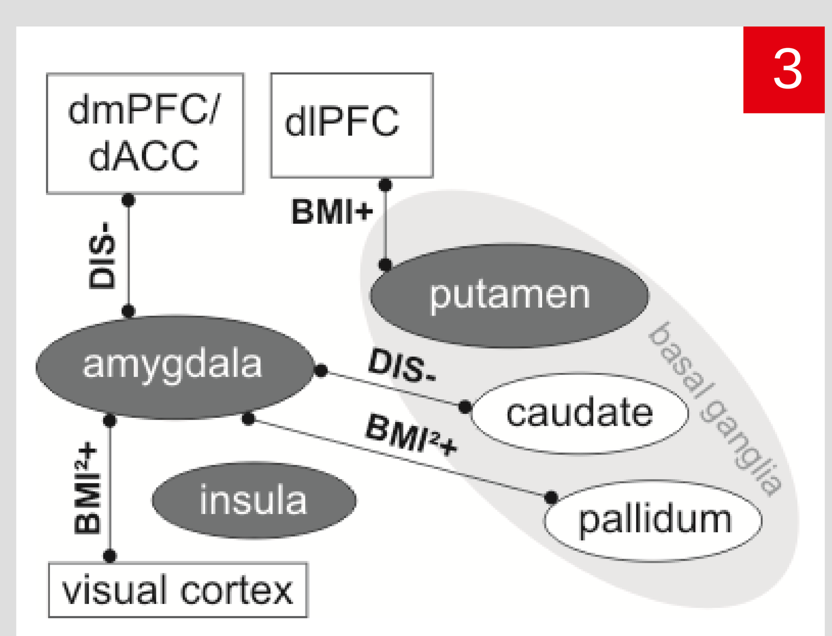

Figure 3: Simplified summary of the relationships shown in Figure 2. Brain mechanisms implicated with the regulation of food craving and their interactions with weight status (BMI) and the individual tendency to overeat (*Disinhibition*, DIS).

Discussion

First study that showed quadratic relationships of food-related brain mechanisms and BMI

Brain activity (BOLD response putamen, amygdala, insula) and BMI

- weight status dependent differences in the motivation to restrict eating

  overweight: chronic weight control[10] → regulation is especially relevant and motivationally salient

  obesity: failure of recognition of negative consequences associated with overeating fattening food (indicated by impaired learning from negative outcomes)[13]

  normal weight: low need for dietary restraint[10]

- alternative explanation: self-control counterproductively enhanced motivation to approach and consume depicted food particularly in overweight individuals as described previously for restrained eaters[14]
- future studies should focus on longitudinal weight development → do relationships translate into successful weight control?
  → if yes, detected regions are potential targets for neurofeedback interventions in the context of obesity.

Functional connectivity putamen/ amygdala and BMI/ eating behavior

- **enhanced PPI putamen/ dlPFC with higher BMI:** stronger need for top-down control[15] on striatal value representation or action selection
- **lower PPI amygdala/ pallidum with overweight** (in comparison to normal weight or obesity): alterations in pleasantness processing[16]
- **lower PPI amygdala/ dmPFC and amygdala/ caudate with higher *Disinhibition*:** hampered self-monitoring[17] and eating-related strategic action planning[18]
  → obese subjects (typically disinhibited eaters) might benefit from approaches strengthening self-monitoring abilities
  → striato-frontal connections might be trained and strengthened with the help of neurofeedback
- ***Cognitive Restraint:*** no associations found (food-deprived state)
  → future studies should modulate internal status
  → dietary restraint might be particularly effective in the sated state when self-control resources are not depleted

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