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EDITORIAL

The potential role of and deficits in frontal cortical brain areas implicated in executive control of food intake

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Following is a series of four papers presenting results from studies examining various aspects of how obesity and images of palatable foods affect brain volumes and neural processing. Together they reflect the increasing sophistication of neuro-imaging paradigms in the study of obesity and focus on the potential role of and deficits in frontal cortical brain areas implicated in executive control of food intake.

Yokum *et al*.[1] report on how body mass index is related to gray matter (GM) and white matter (WM) regional brain volumes in young women and whether these volumes predict weight gain over the subsequent year. The findings demonstrate overall differences in both WM and GM depending upon body mass index (BMI), with obese subjects having lower regional volumes in brain areas implicated in inhibitory controls. Importantly, low GM volumes were related to future weight gain. The data are interpreted to suggest that abnormalities in GM in brain areas associated with inhibitory control increase the risk for weight gain and that abnormalities in WM appear to be secondary to the weight gain.[1]

Similarly, Holsen *et al*.[2] compare patterns of neural activation to food items before and after a meal in normal weight subjects, obese subjects and in individuals with a severe genetic obesity syndrome, Prader–Willi syndrome (PWS). Individuals with PWS are characterized by extreme hyperphagia, that is, if left unchecked, results in severe obesity. In this study, the BMI of the obese and PWS subjects did not differ. Neuroimaging focused on subcortical food motivational circuits (amygdala, nucleus accumbens and hypothalamus) and frontal inhibitory circuitry (dorsolateral, prefrontal and orbitofrontal cortexes). The results demonstrated that the PWS individuals had higher food-item-induced activity in limbic reward areas and lower activity in hypothalamus and hippocampus before the test meal. Following the meal, PWS subjects had higher activity in hypothalamus, amygdala and hippocampus but relatively reduced activity in higher cortical regions. The authors conclude that activity in frontal regions following a meal may be associated with the ability to inhibit food-related behaviors and intake. Thus, in PWS there is dysfunction in dual circuits involved in food reward and decision-making processes regarding food intake, and that the lack of normal cortical activation following a meal in PWS may contribute to their satiety deficits.[2]

As a response to this apparently diminished control over food intake, Hollmann *et al*.[3] report on a study in healthy volunteers designed to examine how instructions to either admit to a desire for food or to actively try to downregulate that desire using a cognitive reappraisal strategy affected patterns of neural activation when shown food items that had been rated for their tastiness and healthiness. The data demonstrate that, under the downregulation condition, there was greater activation in prefrontal-control-related brain areas and in cortical and subcortical regions involved in reward valuation and interoceptive signaling. Furthermore, greater cognitive restraint was associated with greater activation in the dorsolateral prefrontal cortex and the dorsal striatum. The data are interpreted to support the view that an active reappraisal of an unhealthy food recruits brain valuation systems in combination with prefrontal control areas associated with response inhibition, and that individuals with high levels of cognitive restraint show an automatic predisposition to regulate hedonic aspects of feeding.[3]

Finally, Frankort *et al*.[4] report data from a study examining how attention affects reward-related brain activity in satiated overweight and normal weight in response to high-calorie palatable food pictures. They compared patterns of neural activity in response to the pictures when subjects were either not given any instructions or when they were asked to imagine the taste of the food item. Their initial predictions were that there would be more activation in overweight subjects in reward regions and that the difference would be greater in the unbiased viewing (no directions) situation. The data showed a group by condition interaction in food reward processing areas such that, in contrast to the authors' predictions, there was greater activation in the overweight subjects when they were imagining the taste of the foods but lower activation in the unbiased viewing condition. The authors interpret this pattern of results as suggesting roles for both BMI and attention in the reward processing of high-calorie palatable food stimuli, and that the reduced

activation in the overweight in the unbiased viewing condition may reflect avoidance toward the high-calorie foods.[4]

Taken together, these papers suggest that activity in frontal brain regions, following a meal, may be associated with the ability to inhibit post-prandial food-related behaviors and intake. This inhibition is crucial to control energy intake. Inhibition-related frontal region activity appears to be hardly present in obese individuals and in individuals suffering from the PWS.[1,2] Their lack of normal cortical activation following a meal is likely leading to satiety deficits. On the other hand, Hollman *et al*.[3] showed a greater cortical activation in the cognitive-restrained subjects, related to predisposition to control food intake, especially the hedonic effects of it.[3] Rather puzzling are the observations by Frankort *et al*.,[4] introducing diverting effects to pictures of foods that are high or low calorie and have a range in palatability. The observations described in the first two papers partly confirm previous observations,[5–11] that in addition have shown that effects may depend on the severity of obesity, age and sex, leading to the hypothesis that low GM volumes and high WM volumes increase the risk for obesity. Comparable to the reward deficit model of obesity,[12] low GM and high WM volume in reward regions may attenuate reward from food, thus stimulating food intake to achieve reward that, at the same time, is unlikely to be reached.[13] The observation of a similar lack of post-meal cortical brain activity related to inhibition of further eating in the PWS subjects suggests indeed that PWS may be an extreme model of obesity.

The observations by Hollman *et al*.[3] also confirm earlier observations on the contribution of cortical brain activation-related ability to inhibit food intake and thereby energy intake.[13–19] Interestingly, the observations related to obesity, PWS, as well as to dietary restraint, fit well with the suggested bell-shaped reward-addiction–reward-deficiency model.[12,13] Obviously, a possible solution for this, namely dietary restraint behavior, appears to be facilitated by the ability to inhibit, and this ability is related to cortical brain activation.

Conflict of interest

The authors declare no conflict of interest.

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References

1 Yokum S, Ng J, Stice E. Relation of regional gray and white matter volumes to current BMI and future increases in BMI: a prospective MRI study. *Int J Obes Relat Metab Disord* 2012; **36**: 656–664.
2 Holsen LM, Savage CR, Martin LE, Bruce AS, Lepping RJ, Ko E *et al*. Importance of reward and prefrontal circuitry in hunger and satiety: Prader-Willi syndrome vs simple obesity. *Int J Obes Relat Metab Disord* 2012; **36**: 638–647.
3 Hollmann M, Hellrung L, Pleger B, Schloegl H, Kabisch S, Stumvoll M *et al*. Neural correlates of the volitional regulation of the desire for food. *Int J Obes Relat Metab Disord* 2012; **36**: 648–655.
4 Frankort A, Roefs A, Siep N, Roebroeck A, Havermans R, Jansen A. Reward activity in satiated overweight women is decreased during unbiased viewing but increased when imagining taste: an event related f-MRI study. *Int J Obes Relat Metab Disord* 2012; **36**: 627–637.
5 Ward MA, Carlsson CM, Trivedi MA, Sager MA, Johnson SC. The effect of body mass index on global brain volume in middle-aged adults: a cross-sectional study. *BMC Neurol* 2005; **5**: 23.
6 Taki Y, Kinomura S, Sato K, Inoue K, Goto R, Okada K *et al*. Relationship between body mass index and gray matter volume in 1428 healthy individuals. *Obesity* 2008; **16**: 119–124.
7 Pannacciulli N, Del Parigi A, Chen K, Le DS, Reiman EM, Tataranni PA. Brain abnormalities in human obesity: a voxel-based morphometric study. *Neuroimage* 2006; **31**: 1419–1425.
8 Walther K, Birdsill AC, Glisky EL, Ryan L. Structural brain differences and cognitive functioning related to body mass index in older females. *Hum Brain Mapp* 2010; **31**: 1052–1064.
9 Maayan L, Hoogendoorn C, Sweat V, Convit A. Disinhibited eating in obese adolescents is associated with orbitfrontal volume reductions and executive dysfunction. *Obesity* 2011; **19**: 1382–1387.
10 Haltia LT, Viljanen A, Parkkola R, Kemppainen N, Rinne JO, Nuutila P *et al*. White matter expansion in human obesity and the recovering effect of dieting. *J Clin Endocrinol Metab* 2007; **92**: 3278–3284.
11 Raji CA, Ho AJ, Parikshak NN, Becker JT, Lopez OL, Kuller LH *et al*. Brain structure and obesity. *Hum Brain Mapp* 2010; **31**: 353–364.
12 Wang GJ, Volkow ND, Fowler JS. The role of dopamine in motivation for food in humans: implications for obesity. *Expert Opin Ther Targets* 2002; **6**: 601–609.
13 Born JM, Lemmens SG, Martens MJ, Formisano E, Goebel R, Westerterp-Plantenga MS. Differences between liking and wanting signals in the human brain and relations with cognitive dietary restraint and body mass index. *Am J Clin Nutr* 2011; **94**: 392–403.
14 Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the vmPFC valuation system. *Science* 2009; **646**: 646–648.
15 Cornier M-A, Salzberg AK, Endly DC, Bessesen DH, Tregellas JR. Sex-based differences in the behavioral and neuronal responses to food. *Physiol Behav* 2010; **99**: 538–543.
16 Miller EK. The prefrontal cortex and cognitive control. *Nat Rev Neurosci* 2000; **1**: 59–65.
17 Tanji J, Hoshi E. Role of the lateral prefrontal cortex in executive behavioral control. *Physiol Rev* 2008; **88**: 37–57.
18 DelParigi A, Chen K, Salbe AD, Hill JO, Wing RR, Reiman EM *et al*. Successful dieters have increased neural activity in cortical areas involved in the control of behavior. *Int J Obes* 2007; **31**: 440–448.
19 Davids S, Lauffer H, Thoms K, Jagdhuhn M, Hirschfeld H, Domin M *et al*. Increased dorsolateral prefrontal cortex activation in obese children during observation of food stimuli. *Int J Obes* 2010; **34**: 94–104.