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Research Report

# Reduced nucleus accumbens and caudate nucleus activation to a pleasant taste is associated with obesity in older adults

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ABSTRACT

Although obesity is recognized as a global health epidemic, insufficient research has been directed to understanding the rising prevalence of obesity in the fastest growing segment of the population, older adults. Late-life obesity has been linked to declines in physical health and cognitive function, with implications not only for the individual, but also for society. We investigated the hypothesis that altered brain responses to food reward is associated with obesity, using fMRI of response to pleasant and aversive taste stimuli in young and older adults performing a hedonic evaluation task. Correlations between higher levels of abdominal fat/body mass index and reduced fMRI activation to sucrose in dopamine-related brain regions (caudate, nucleus accumbens) were large in older adults. Significant associations between a hypofunctioning reward response and obesity suggest the hypothesis that decreased dopamine functioning may be a plausible mechanism for weight gain in older adults.



## 1. Introduction

Obesity has become a global health epidemic. The World Health Organization estimated that in 2005 approximately 400 million adults were obese and this number is projected to increase to more than 700 million by 2015 (World Health Organization, 2006).

Obesity in older adults is increasing, with the prevalence of obese individuals over the age of 60 estimated to reach 37.4% in 2010 (Arterburn et al., 2004). Older adults are at an increased risk for weight gain due to muscle loss, a slowing metabolism, and reductions in energy expenditure (Villareal et al., 2005). Additionally, late-life obesity can exacerbate age-related declines in physiological and cognitive health (Beydoun et al., 2008; Jenkins, 2004; Yaffe et al., 2004), impairing life quality and substantially increasing healthcare costs and burdens to society. Although it is recognized that obesity among older adults is a significant issue, the underlying mechanisms still remain to be elucidated.

Weight gain is largely affected by caloric intake (Sherwood et al., 2000) and a critical factor driving dietary selection and energy consumption is food reward (Saper et al., 2002; Wang et al., 2001). In addition to a drive to achieve energy balance, motivation to eat is commonly influenced by pleasure and enjoyment (Berthound, 2007), and foods that are highly pleasant tend to have high energy densities (Drewnowski, 1998) and elevated sugar and fat content (Drewnowski and Greenwood, 1983). An individual's perception of the sensory properties of food is modulated by physiological state; therefore, greater reward is experienced during hunger (Cabanac, 1971; Haase et al., 2009; Kringelbach et al., 2003; Rolls et al., 1989; Seymour and Dolan, 2008; Small et al., 2001). This shift in reward

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value that occurs during the satiation process is a physiological signal for meal termination (Cabanac, 1971; Hetherington, 1996). However, with the rising availability of energy-dense foods in combination with food industry technologies that increase food palatability, these physiological signals may not be sufficient to induce meal termination, resulting in excess caloric intake (Rolls, 2007; Seymour and Dolan, 2008).

Elucidating neural substrates of food reward and relationships between cortical responses to food-related stimuli and obesity may provide further insight into the development and maintenance of obesity. Researchers have noted aberrant responses in obese individuals in the nucleus accumbens, orbitofrontal cortex, insula, and amygdala in response to food pictures (Rothemund et al., 2007; Stoeckel et al., 2008) and Tomasi et al. (2009) reported negative correlations between BMI and BOLD responses during gastric distention in dopaminergic brain regions (e.g., amygdala, anterior insula). This suggests the possibility that the responses to food stimuli in cortical regions involved in higher-order taste processing that modulate the experience of reward may be altered in overweight individuals.

Obesity has been compared to addiction because overeating and substance abuse are both driven by reward (Volkow et al., 2008). The mesolimbic dopamine (DA) system plays an important role in the regulation of energy intake by modulating the experience of food reward (Martel and Fantino, 1996). Pharmacological research has shown that DA receptor agonists suppress appetite and lead to weight loss (Leddy et al., 2004; Towell et al., 1988) while DA antagonists tend to increase appetite and lead to weight gain (Baptista, 1999). Therefore, it has been hypothesized that differential activation of the DA system and a reward deficiency syndrome may be a key factor in understanding the biological basis of addictive behaviors, including overeating (Blum et al., 1990; Volkow et al., 2008). Specifically, insufficient stimulation of the DA system may be a risk factor for weight gain.

There is preliminary neuroimaging evidence in support of this hypothesis. Recently, Stice et al. (2008a) showed a relationship between a blunted caudate response to a pleasant food stimulus and obesity in young adults and adolescent females, which was moderated by the Taq1A A1 Allele, (considered to be associated with decreased D2 receptor availability). In line with this hypothesis, we expected to find relationships in young adults between obesity and decreased activation in regions receiving dopaminergic input (caudate, nucleus accumbens, and amygdala) in response to a pleasant taste that were greater when they were hungry, and reward value would be increased, than when they were satiated.

The relationship between food reward and obesity is unknown in older adults. The aging process is associated with pronounced declines in dopamine concentration and receptor density in the prefrontal cortex and striatum (Bäckman and Farde, 2005). Therefore, we hypothesized that due to greater variability in declines of the dopamine reward response in the older adult sample (spanning from individuals in their mid-60s to individuals in their late 80s), stronger negative correlations between cortical activation and obesity would be demonstrated in older adults.

We used functional magnetic resonance imaging (fMRI) during the physiological states of hunger and satiety to investigate relationships between neural correlates of reward and abdominal obesity. Using this paradigm, we have found increased activation to sucrose in the no-preload condition in reward-related brain regions including the caudate nucleus and amygdala, in both young (Haase et al., 2009) and older adults (Jacobson et al., 2010). Because these regions are involved in the motivation for and reinforcing effects of eating, we hypothesized that the intensity of the responses in these regions during taste stimulation and hedonic evaluation would vary according to metabolic status. Specifically, we hypothesized that: (1) activation of the caudate nucleus and mesolimbic dopamine pathway (specifically, amygdala, and nucleus accumbens) would be associated with waist circumference and body mass index (BMI) for both age groups, (2) greater levels of abdominal fat/higher BMIs would be accompanied by a reduced reward response (i.e., less fMRI activation), and (3) due to greater variability in DA functioning, these relationships would be more robust in older adults.

## 2. Results

### 2.1. Demographics

One-way analyses of variance (ANOVAs) were run to examine potential demographic differences between the age groups of young and older adults. There were no differences in height, $F(1,37)=0.12$, $p=0.73$, or weight, $F(1,37)=2.18$, $p=0.15$, between young and older adults. Older adults had higher BMIs ($M=27.51$, $SD=2.88$) compared to the young adults ($M=24.45$, $SD=3.63$), $F(1,37)=8.55$, $p=0.006$. Levene's Test was nonsignificant, indicating equal variance in BMIs across age group ($p=0.189$). The ranges of BMI values were very similar in both age groups. In young adults, the BMI ranged from a minimum of 19 to a maximum of 32. In older adults, the BMI ranged from a minimum of 21 to a maximum of 33.

In addition, waist circumference (cm) was significantly larger for older adults ($M=95.02$, $SD=9.78$) compared to younger adults, ($M=85.22$, $SD=9.94$) $F(1,37)=9.64$, $p=0.004$. Levene's Test was nonsignificant, indicating equal variance in waist circumferences across age group ($p=0.917$). In young adults, the waist circumference ranged from a minimum of 67 cm to a maximum of 104 cm. In older adults, the BMI ranged from a minimum of 77 to a maximum of 113.

Between subjects, two-way ANOVA was used to examine potential differences in levels of exercise using the short form of the International Physical Activity Questionnaire and age and BMI group (using BMIs of 25 for young adults and 28 for older adults as cutoffs) as factors. One participant did not fill out the questionnaire, so the analysis is based on the remaining 38 participants. There were no main effects of age, BMI group, or interaction between the two for physical activity levels, $F(3,36)0.615$, $p=0.61$.

### 2.2. Psychophysics

#### 2.2.1. Hunger ratings

Hunger ratings were recorded pre- and post-fMRI scan using a modified version of the general labeled magnitude scale (gLMS; Green et al., 1993; Green et al., 1996; Bartoshuk et al., 2004). Additionally, in the preload condition, hunger ratings were