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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.

Keywords

reward value; taste; gustatory; nucleus accumbens; caudate; fMRI

1. Introduction

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

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Author Contributions

C.M. directed the project; E.G., L.H. and C.M. designed the experiment; E.G., A.J. and L.H. collected and analyzed data; E.G. and C.M. wrote the manuscript.

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 & 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 & Dolan, 2008; Small et al., 2001). This shift in reward 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 & 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 and colleagues (2009) reported negative correlations between BMI and BOLD response 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 & 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 and colleagues (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 TaqIA 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, $F(1, 37) = .12$, $p = .73$, or weight, $F(1, 37) = 2.18$, $p = .15$, 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), $F(1,37) = 8.55$, $p = .006$. Levene's Test was nonsignificant, indicating equal variance in BMIs across age group ($p = .189$). 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) $F(1,37) = 9.64$, $p = .004$. Levene's Test was nonsignificant, indicating equal variance in waist circumferences across age group ($p = .917$). In young adults, the waist circumference ranged from a minimum of 67cm to a maximum of 104cm. In older adults, the BMI ranged from a minimum of 77cm 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, $F(3,36) = .615$, $p = .61$.

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 taken before and after consumption of a nutritional preload prior to entering the scanner. Upon primary inspection, the nutritional preload was significant in lowering hunger ratings from pre- (M = 29.31, SD = 23.85) to 10 minutes post-consumption (M = 9.23, SD = 15.21), $F(1,38) = 50.70$, $p < .001$. However, to determine the effect of age group and metabolic status on hunger ratings before and after the preload, a 2×2 split-plot design was run using age as a between-group variable and waist circumference as a covariate. There was a main effect of age, $F(1, 36) = 8.64$, $p = .006$, on overall hunger ratings. Older adults were generally less hungry (M = 12.4, SE = 3.6) than younger adults (M = 26.5, SE = 3.7). There were no significant age x preload condition, $F(1,36) = 1.64$, $p = .21$, or waist circumference x preload condition, $F(1,36) = 1.00$, $p = .32$, interactions. Additionally, when age and waist circumference were included in the model, the effect of preload condition approached, but did not reach significance, $F(1, 36) = 3.19$, $p = .08$. A positive correlation between waist circumference and difference scores relating to the decrease in hunger pre- and post-preload approached, but did not reach statistical significance (r = .28 , $p = 086$).

2.2.2 Pleasantness Ratings—Participants also rated the pleasantness of the caffeine and sucrose solutions before and after the preload (before the satiety scan), using a modified version of the gLMS. A split-plot design was used to compare pleasantness ratings for the two stimuli (caffeine and sucrose), across physiological state (hunger and satiety), and between the age groups. There was a main effect for stimulus, $F(1, 37) = 138.36$, $p < .001$; sucrose (M = 59.88, SD = 8.86) was considered to be more pleasant than caffeine (M = 35.26, SD = 9.05) by both age groups averaged across physiological state. There were no main effects for age group ($p = .721$) or preload condition ($p = .110$). Additionally, no significant stimulus by age group ($p = .172$), stimulus by preload condition ($p = .675$), or stimulus by preload condition by age group ($p = .792$) interactions were found.

2.2.3 Intensity Ratings—To determine whether there were any differences in perceived intensity of the stimuli, magnitude estimates of intensity were also recorded using the gLMS prior to entering the scanner. There were no differences in intensity estimates for caffeine between the two age groups, $F(1, 37) = .855$, $p = .36$, (M = 33.59, SD = 16.67). However, older adults (M = 35.30, SD = 15.31) reported the sucrose to be more intense compared to the young adults (M = 23.74, SD = 8.65), $F(1, 37) = 8.31$, $p = .007$.

2.3 Functional Neuroimaging

For the purpose of this paper, only associations between abdominal fat/BMI and brain activity in response to caffeine and sucrose are reported. Neuroimaging data were collected as part of a larger study and differences in activation patterns between the two age groups are reported in Jacobson et al., (2010).

A region of interest (ROI) analysis yielded parameter estimates (fit coefficients) corresponding to brain activation in each specified ROI calculated separately for each of the four conditions (i.e., no-preload/caffeine, preload/caffeine, no-preload/sucrose, and preload/sucrose). For example, in the preload/caffeine condition, fit coefficients for each participant were calculated using brain activation in response to the caffeine stimulus during the preload condition for each specified ROI. The 5 brain regions used in this analysis were anatomically defined and selected based on a priori hypotheses and the literature on food reward and hunger modulation (Haase et al., 2009; Rolls et al., 1989; Stice et al., 2008a,b).

Correlations were run between fit coefficients and both waist circumference and BMI separately for young and older adults. Waist circumference and BMI were significantly correlated for both the young ($r = .76$, $p < .001$) and older adults ($r = .63$, $p = .003$). Statistically significant correlations between waist circumference or BMI, and brain activity in the no-preload/sucrose condition are shown in Table 1. A test-wise error rate of .005 was used to determine statistical significance after correcting for multiple statistical tests.

For the young adults in the no-preload/sucrose condition, significant negative associations were only present between waist circumference and brain activity bilaterally in the caudate body. There were no other significant associations between waist circumference or BMI and brain activation to sucrose in the no-preload or preload condition. Additionally, there were no significant associations between BMI or waist circumference and brain activation to caffeine in young adults during the no-preload or preload conditions.

In older adults during the no-preload/sucrose condition, a large negative association between waist circumference and brain activation in the right amygdala, approaching statistical significance ($p = .01$) is displayed in Fig. 1a (See also Table 1). Significant negative associations were present in this condition between waist circumference and brain activation in right caudate head, body and tail (Fig. 1b), and left nucleus accumbens (Fig. 1c). Reduced right caudate tail and right nucleus accumbens activity were also associated with larger BMI in the older adults during the no preload condition. No associations were present in older adults between brain activity to sucrose in the specified ROIs and BMI or waist circumference during the preload condition. Similarly, there were no significant associations between waist circumference/BMI and brain activation in ROIs to caffeine for older adults in the preload or no preload conditions.

3. Discussion

To date, the literature addressing food reward representation in the primate brain has focused on young adults and the dissociations between the neural substrates of “liking” and “wanting” (O’Doherty et al., 2002; Small et al., 2008; Stice et al., 2008b; for reviews see Berridge 1996; Berridge et al., 2009; and Peciña, 2008), differential cortical activation by motivational state (Critchley & Rolls, 1996; de Araujo et al., 2003a; Haase et al., 2009; O’Doherty et al., 2000; Rolls et al., 1989; Seymour & Dolan, 2008; Small et al., 2001), and neural correlates of pleasantness ratings (Anderson et al., 2003; de Araujo et al., 2003b; Grabenhorst et al., 2009; Rolls et al., 2003; Small et al., 2003).

In this study, we used a manipulation of motivational state (preload v. no-preload conditions), a bitter, unpleasant taste (caffeine), a sweet, pleasant, food-related taste (sucrose), and a hedonic evaluation task specifically to investigate relationships between cortical activation of regions linked to reward value and obesity in older adults. We found significant negative linear relationships between levels of abdominal fat, BMI and fMRI activity in the caudate nucleus during gustatory stimulation and subsequent hedonic evaluation for both young controls and older adults. Importantly, in older adults, activation of the nucleus accumbens, an essential structure involved in the brain’s reward system, was also negatively related to waist circumference measurements and BMI in the no-preload/sucrose condition. In young adults, no relationship was present between nucleus accumbens activation and waist circumference or BMI in the no-preload/sucrose condition.

All significant correlations between waist circumference/BMI and brain activity in ROIs were in response to the sucrose stimulus during the physiological state of hunger. Regions involved in motivation and food hedonics are differentially activated with respect to physiological condition (Critchley & Rolls, 1996; O’Doherty et al., 2000; Rolls et al., 1989;

Seymour & Dolan, 2008; Small et al., 2001), and we have recently shown greater activation in the insula, orbitofrontal cortex, and amygdala during the hunger relative to the preload condition in response to sucrose in young adults (Haase et al., 2009).

Physiological mechanisms related to the experience of food reward and hedonics may have a substantial impact on resulting behaviors including meal initiation and termination. While many factors (e.g. genetics and environment) are likely involved in the development of obesity, links between cortical activation in response to a pleasant taste and levels of abdominal fat or BMI support an underlying biological basis for obesity. Additionally, age-associated disruptions in networks integral to reward processing (Dreher et al., 2008; Mell et al., 2009), may affect energy consumption in older adults.

Both age groups demonstrated relationships between brain activity and waist circumference that were negative in direction. Less brain activation in dopamine-related regions was related to larger amounts of abdominal fat in young and older adults. Reward deficiency syndrome (Blum et al., 1990) refers to a condition in which reduced dopaminergic functioning results in a suppressed reward response. Individuals are then hypothesized to compensate by seeking out quickly rewarding stimuli like sweet foods, drugs, or sex. Specifically, D2 DA receptors play an important role in the modulation of reward-related behaviors. D2/D3 agonist administration greatly reduces rats' preference for chocolate (Cooper & Al-Naser, 2006), and D2 receptor levels are decreased in the striatum of pathologically obese individuals (Wang et al., 2001). In addition, the A1 allele of the Taq1A polymorphism (rs1800497) has been identified as a possible genetic risk factor for obesity. Specifically, the A1 allele is associated with reduced D2 striatal receptor densities (Pohjalainen et al, 1998; Thompson et al., 1997) as well as with obesity (Noble et al., 1994; Spitz et al., 2000). The association between low D2 receptor densities in reward pathways of the brain and obesity provides further evidence in support of a physiological mechanism underlying weight gain and obesity.

To date, relationships between cortical processing of food reward and levels of body fat have not been examined in older adults. We have recently found fMRI activation to pure tastes in gustatory and reward-related brain regions in both young and older adults, with older adults demonstrating activation patterns that are consistent with an hypothesis of age-related compensation (Jacobson et al., 2010). Interestingly, when hungry, and thus when food-related stimuli are theoretically more rewarding, older adults showed a relationship between less nucleus accumbens activity and greater levels of abdominal fat/BMI. Dopamine action in limbic areas, especially the nucleus accumbens and amygdala, is considered to be a key factor in the reinforcing effects of both addictive drugs (Koob & Bloom, 1988) and highly palatable food (Comings & Blum, 2000; Martel & Fantino, 1996). Food consumption causes increases in nucleus accumbens DA activity, similar to alcohol intake and drug administration (Bassareo & Di Chiara, 1999). Dopamine activity in the nucleus accumbens then triggers activation of the mesocorticolimbic reward pathways of the brain resulting in reinforcement of the behavior (Hoebel, 1985).

Aging is associated with declines in the DA system (Kaasinen et al., 2000; Volkow et al., 1998; 2000), including significant losses in D2 receptor levels (Joseph et al., 1990), which may result in altered reward processing (Dreher et al., 2008). In addition to substantial decreases in DA function, chemosensory declines and changes in appetite likely affect food reward in older adults (Schiffman & Graham, 2000). Therefore, we speculate that older adults may be especially at risk for reward-deficiency syndrome and weight gain.

Although DA levels were not directly measured, the blood-oxygen level dependent (BOLD) response recorded using fMRI is considered to be directly coupled to DA activity

(D'Ardenne et al., 2008; Knutson & Gibbs, 2007). Additionally, it is important to note that a limitation of correlation analyses is the lack of ability to ascertain the direction of significant relationships. An alternative to the hypothesis of increased energy intake as a consequence of a suppressed reward response is the hypothesis that food-related stimuli become less rewarding after an unhealthy accumulation of abdominal fat. In other words, decreased dopamine functioning may be an outcome of overeating; a mechanism where food-related stimuli are less rewarding due to a physiological need to decrease energy intake.

There are limitations to the study. The two age groups may differ in energy requirements, although they received the same preload. Therefore, it is possible that the preload may have exceeded the energy requirements of some participants. However, the nutritional intervention was aimed at inducing a low-motivation/sated physiological state, and psychophysical hunger ratings of both age groups demonstrated that the intervention was successful. Additionally, a small number of participants reported smoking cigarettes, although none were heavy smokers (> 20 cigarettes per day). Finally, Mulderink and colleagues (2002) reported an effect of acute caffeine administration on the BOLD response. However, they administered 200 mg of caffeine in one dose and waited over 30 minutes to observe the delayed effect; while the current participants received, intermittently and over the duration of an entire scan (approximately 30 minutes), at most 18.6 mg of caffeine.

There was a non-significant trend towards a positive relationship between waist circumference and the decrease in hunger ratings pre- and post-preload. Taste intensity of sucrose was rated higher by older than younger adults, although there were no differences in caffeine ratings. It is possible that differences in perceived intensity may have contributed to the age-specific effects observed. In addition, there are other physiological variables that are involved in the satiety process (e.g., hormones involved in feeding regulation), obesity (e.g., hypertension, LDL and HDL blood levels, etc.), and lifestyle choices (e.g., alcohol consumption) not measured in this study that may impact participants' brain response to taste stimuli during the states of hunger and satiety. Further understanding of potential age-related differences in taste intensity, the effects of hunger and satiety on reward processes in the brain, and associations between these effects and obesity will require incorporation of many additional factors into the experimental design of future studies.

In summary, this investigation provides the first evidence that BMI and abdominal fat, specifically in older adults, is associated with neural activity in areas involved in food reward. Additional investigation into brain behavior associations may reveal identifiable risk factors for weight gain in young and older adults. A strong relationship between reduced nucleus accumbens activity and abdominal obesity in older adults suggests that this age group may be particularly at risk for weight gain. We speculate that this may be related to age-related declines in D2 receptors levels and a hypofunctioning reward system.

4. Experimental Procedure

A detailed description of the protocol and the system for delivering taste stimuli in the fMRI environment used in the study are outlined in the Journal of Neuroscience Methods (Haase et al., 2007).

4.1 Participants

Twenty healthy older adults ranging from 65 to 87 years of age (M = 73, S.D. = 6.74) and twenty healthy young adults ranging from 18 to 29 years of age (M = 23.6, S.D. = 2.66) were recruited from the San Diego community. Participants gave informed consent and received monetary compensation for their participation. Data from one young participant were discarded due to signal dropout during the scanning session. Of the remaining

participants, 3 of the older adults and 5 of the young adults reported being current smokers. Participants did not smoke within two hours of the scan; none reported heavy smoking (> 20 cigarettes per day); and there were no differences in taste threshold between smokers and nonsmokers, $F(1,37) = .310$, $p = .581$. The Institutional Review Boards at both San Diego State University and the University of California, San Diego gave approval for the study. Each subject participated in three separate sessions detailed in the following sections.

4.2 Screening Session

During the first session, participants were screened for exclusionary criteria including ageuesia, anosmia, and upper respiratory infection or allergies within the prior two weeks (Harris et al., 2006; Murphy et al., 2002). Taste thresholds for all participants were assessed using a forced choice procedure with a series of varying concentrations (.0032M to .36M) of sucrose solutions (Murphy et al., 1990). Odor threshold was assessed using a forced-choice, procedure with varying concentrations of n-butyl alcohol presented monorhinically (Murphy et al., 1990). Older adults were also screened for dementia using both the Mini-Mental State Examination (Folstein et al., 1975) and the Dementia Rating Scale (Mattis, 1984).

To assess waist circumference, each participant's waist was measured at the midpoint between the highest point of the iliac crest and the lowest point of the rib cage. Body mass index (BMI) was calculated by dividing each participant's weight by the square of his or her height (Kg/cm^2). The short form of the International Physical Activity Questionnaire was used to assess physical activity levels (Craig et al., 2003).

4.3 Neuroimaging Procedure

The neuroimaging was done over two separate sessions using functional magnetic resonance imaging. The purpose of having two fMRI sessions was to investigate brain activation both during a physiological state of hunger (no-preload condition) and a physiological state of satiety (preload condition). Participants fasted for 12 hours prior to each scanning session and rated their perceived hunger and the pleasantness of the stimuli using the gLMS prior to entering the scanner on both days. In the preload condition, participants rated their hunger and the stimuli both before and after consuming a nutritional preload containing 700 kcal (vanilla-flavored Ensure Plus).

4.3.1 Stimulus Delivery—Because the present study was designed to investigate the association between measures of obesity and activation to taste stimuli that fall at the ends of the spectrum of pleasantness and aversion of the hedonics of taste qualities, we analyzed activation to sucrose (0.64M; sweet) and caffeine (0.04M; bitter) presented as aqueous solutions. Participants lay supine in the scanner and were fitted with a bite bar to minimize head movement, including that associated with swallowing, and to allow the tubing for taste delivery to rest comfortably between the lips. The stimuli were individually filled in syringes and delivered to the tongue of the participant through 25-foot long tubing connected to programmable pumps located in the operator room. The computer-programmed syringe pumps, triggered by the scanning computer, pushed the syringes so that 0.3 ml of solution was presented in 1 sec from each syringe. Each stimulus was delivered 8 separate times for each functional run, presented pseudo-randomly with a 10s ISI. Distilled water was presented twice after each stimulus, the first time as a rinse and the second as a baseline comparison for the solution, resulting in a minimum separation of 60 seconds before the same stimulus was presented again (discounting the water delivery, no stimulus was presented twice in a row). This procedure was designed to minimize habituation and adaptation of the gustatory system.

4.3.2 Data Acquisition—The neuroimaging sessions were performed at the Center for Functional Magnetic Resonance Imaging at the University of California, San Diego using a 3T GE Signa EXCITE Short-Bore research scanner. Structural images for anatomical localization of functional images were collected before each functional scan using a high-resolution T1-weighted whole-brain MP-RAGE sequence (Field of view (FOV) = 25cm, slice thickness = 1mm, resolution 1×1×1 mm^3, echo time (TE) = 30ms, Locs per slab = 136, flip angel = 15°). A whole brain gradient echo planer pulse sequence was used to acquire T2*-weighted functional images (24 axial slices, FOV = 19cm, matrix size = 64×64, spatial resolution = 3×3×3 mm^3, flip angle = 90°, echo time (TE) = 30ms, repetition time (TR) = 2000ms).

4.3.3 Image Analysis—Functional data were processed using Analysis of Functional NeuroImage (AFNI) software (Cox, 1996). Pre-processing consisted of motion correction, temporal and spatial smoothing, concatenation and automasking. For motion correction, 3dregistration in AFNI was used to correct for small head movements. Temporal smoothing averaged the surrounding time points using the program 3dTsmooth. 3dmerge was used for spatial smoothing. Next, concatenation of the runs was done using 3dTcat and voxels outside of the brain (noise) were clipped using 3dautomask (Cox, 1996). Each individual brain was transformed into Talaraich space to aid in controlling for individual structural differences and to help reduce error in the group analyses.

4.3.4 Data Analysis—At the individual level, processing consisted of deconvolution applied to the concatenated runs using 3dDeconvolve within AFNI (Cox, 1996). Deconvolution is a multiple regression analysis used for fMRI data with the purpose of fitting specific time points with distinct coefficients representing an estimate of the impulse response function for each voxel. Deconvolution was used to fit each voxel's time series to an activation model (based on the specified input contrasts defined below) and then test these models for significance. This estimate was given as an output statistic (for each voxel) called the fit coefficient, which is synonymous to a beta coefficient. Also specified in the deconvolution analysis was a baseline consisting of an average of the activation during the second water presentation after each stimulus presentation.

A region of interest (ROI) analysis was then run on the fMRI data from each individual using 5 regions in both hemispheres for each of the 4 contrasts (caffeine in the hunger condition, caffeine in the satiated condition, sucrose in the hunger condition and sucrose in the satiated condition). The ROI analysis was conducted using 3dROIstats within AFNI (Cox, 1996). The purpose of the program is to display means over masked regions. The regions used for this analysis were the caudate nucleus (separated into tail, body, and head), nucleus accumbens, and amygdala. The anatomical border for each region was defined by AFNI using the Talairach Daemon database.

For each individual, masks of the selected ROIs were applied to the processed functional MRI datasets so that the voxels located in the ROIs could be isolated and the mean fit coefficients over this predefined volume could be extracted. Several participants had significant signal dropout in the nucleus accumbens and these data were excluded from the analyses.

The ROI analysis yielded fit coefficient values corresponding to each ROI for each individual in each condition. At the group level, data were analyzed using zero-order correlations between the averages calculated from defined ROIs and waist circumferences and BMIs to determine if relationships were present for each age group separately.

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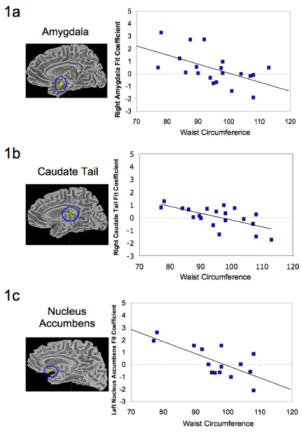

Figure 1.

(a) Association between waist circumference (cm) and right amygdala activation in older adults (R^2 = .32). (b) Association between waist circumference (cm) and right caudate tail activation in older adults (R^2 = .43). (c) Association between waist circumference (cm) and left nucleus accumbens activation in older adults (R^2 = .52).

Table 1

Significant Correlations between Waist Circumference/BMI and ROIs for *SUCROSE* during the No-Preload Condition.

	WAIST CIRCUMFERENCE/BMI		
		Young Adults	**Older Adults**
L	**CAUDATE HEAD**		
R			**r = −.60, *p* = .005**
L	**CAUDATE BODY**	**r = −.61, *p* = .005**	
R		**r = −.61, *p* = .005**	**r = −.63, *p* = .003**
L	**CAUDATE TAIL**		
R			**r = −.65, *p*= .002** ***r = −.61, *p*= .004**
L	**NUCLEUS ACCUMBENS**		**r = −.72, *p* = .002**
R			***r = −.78, *p* = .001**
L	**AMYGDALA**		
R			****r = −.56, *p* = .010**

Significance is set at $p \leq 0.005$; most nonsignificant correlations are not shown.

Abbreviations: L = left, R = right, BA = Brodmann Area.

r: Correlation represents relationship between fMRI activation and waist circumference.

* r: Correlation represents relationship between fMRI activation and BMI.

** r: Correlation between waist circumference and brain activation did not reach statistical significance.