DEFICIENCIES IN INHIBITORY MECHANISM IN OBESITY

by

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ABSTRACT

Theories of human obesity often refer to deficiencies in inhibitory control. An important component of inhibitory control is the ability to make on-the-fly adjustments like those required when interference is encountered or when a prepotent response needs to be interrupted (Barch et al., 2009). The inhibition of an ongoing response is frequently studied using the stop signal reaction time (SSRT) task. An SSRT task is normally a choice reaction time task with embedded trials in which a 'Stop' signal appears and requires that the subject completely inhibit a response initiated to one of the 'Go' signals. The time required to stop is computed and ERPs associated with the stop signal can be recorded (deJong et al., 2000). While many studies point to a general inhibitory deficit in obesity, the question remains whether food stimuli are linked to even greater deficits in obese individuals. By varying the content of the 'Go' signal, it may be possible to determine whether inhibitory control deficits associated with obesity are greater to food cues. The present experiment was designed to address this issue. ERPs were recorded while fifty-six obese and normal weight undergraduates performed an SSRT task in which 'Go' signals were either neutral pictures or highly appetitive positive pictures including high calorie, high fat foods. No behavioral differences were found between the two groups. In control subjects, successful stop trials were associated with larger P300s than were the unsuccessful stop trials, though this P300 difference was absent in the obese subjects. In the obese group, no differences were found among the stimuli, suggesting that the inhibitory control deficit is general and that food is not linked with greater inhibitory difficulties.

Chapter 1

INTRODUCTION

It has been noted that obesity and addiction have many functional similarities. Neuroimaging studies suggest than an altered functioning of the brain's reward system is linked to the etiology and maintenance of both obesity and addiction (Volkow & Wise, 2005; Wang et al., 2001). Two particular models of addiction help explain how obesity functions. The first model, the incentive sensitization model, assumes that sensitization of the dopaminergic reward system is associated with salience attribution to reward cues (e.g. drugs or food), making the cues more appealing, which, in turn, leads to craving and intake of the rewarding substance (Berridge, 2007). The second model, the impaired response inhibition and salience attribution model, suggests that addiction is not only characterized by increased saliency to reward stimuli but also by inhibitory control deficits that lead to a loss of self-directed behavior (Goldstein & Volkow, 2002). Though these models have been explored in addiction, these models have not been fully assessed in obesity. Specifically to obesity, only a few studies have investigated the relationship between food, rewarding stimuli in general, and impaired response inhibition in obesity.

Although there are some behavioral studies illustrating a negative association between obesity and inhibitory control in general (Chalmers, Bowyer, & Olenick, 1990; Nederkoorn, Braet, Van Eijs, Tanghe, & Jansen, 2006; Nederkoorn, Jansen, Mulkens & Jansen, 2007; Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006; Rydén et al., 2003), there are very few studies that assess inhibitory deficits that might be specific to food associated stimuli. Seeing that food is more positive and arousing to obese individuals than to controls (Saelens, 1996; Epstein et al., 2007), it is plausible that food may be linked to greater inhibitory

difficulties. Similar to the role of drugs in addiction, food acts as the rewarding stimulus in obesity and this increased saliency of food may impact response inhibition. Of the few behavioral studies that have investigated food-specific inhibitory impairments in obesity, the evidence is mixed and there is no consensus yet on whether food is related to greater inhibitory impairment than non-food associated stimuli in obese participants. For example, Soetens and Braet (2007) administered an imbedded work task (IWT) containing high caloric food and control words to overweight and normal-weight adolescents in order to measure attention interference. The task consisted of a letter grid with hidden words, specifically 12 high-caloric food words and 12 control words, and the adolescents were asked to survey the grid and see which words come into vision and then write those words down in order they were found. They found no differences in the processing of food associated or control words in overweight or normal-weight adolescents. Likewise, Loeber and colleagues (2012) administered a behavioral Go/No-Go task with food associated and neutral words to obese and normal-weight individuals. Participants were instructed to respond to the words of the target category (either the food-associated or object words) as quickly as possible by pressing the space bar during the 'Go' trials, but to inhibit their respond when distractors (the other group of words) were presented during the 'No-Go' trials. They also found no differences between the two groups. Rather, they found faster reaction times and inhibitory impairment in response to food associated stimuli relative to neutral words in both groups.

On the contrary, however, Braet and Crombez (2003) found that food affected obese children more than control children. In their experiment, obese and control children completed a Stroop task, which included food associated words, negative-emotion words, and control words. The children were instructed to state aloud the color of each word as quickly and accurately as

possible and to ignore the meaning of each word. They found that obese children were slower in naming the color of food words compared to when naming control words. Their results demonstrated that food associated words caused more interference in obese children but not in their normal-weight peers. Although both Soetens and Braet (2007) and Braet and Crombez (2003) examined interference effects of food in obesity, the differences in results may have been due to the use of tasks that do not analyze both approach and inhibitory behaviors. The IWT measured more of the approach aspect while the Stroop task measured more of the inhibitory feature of response inhibition. Therefore, it would be better to utilize the Stop Signal Reaction Time (SSRT) task. The SSRT task examines an individual's ability to withhold an already triggered motor response (Logan et al., 1997) and with both 'Go' and 'Stop' trials, is capable of assessing both approach and inhibitory behaviors, and is more suited to determining whether food is associated with both increased saliency and greater inhibitory impairment in obesity. In addition, another factor that may have led to the differences in results between the two studies was that Braet and Crombez included high-caloric and healthy food words, while Soetens and Braet included only high-caloric food words. Although Braet and Crombez included another condition, both experiments lacked a non-food associated control condition, which would help to examine whether the deficits are greater to food relative to neutral cues. In order to assess whether food is associated with greater inhibitory impairment in obese individuals, studies should include both food-specific stimuli as well as non-food associated stimuli.

Complimenting behavioral techniques, electrophysiological and neuroimaging methodology has also been brought to bear on the study of subjects characterized by difficulties with inhibitory control. Using event-related brain potentials (ERPs), Liotti and colleagues (2005) and Kamijo and colleagues (2012) found inhibitory control deficiencies in children with

ADHD and obesity, respectively, when compared to their normal control counterparts. ERPs are becoming widely used in response inhibition studies as they provide a noninvasive and temporally specific way to analyze the processes associated with successful inhibitory control. In studies that employ the SSRT task to investigate inhibitory control, the two ERP components of the greatest relevance are the N200 and P300. The N200 component is a negative deflection in the waveform that occurs approximately 200 ms after the onset of the stop signal, and is believed to be generated in the right inferior frontal cortex (Pliszka, Liotti, & Woldorff, 2000). The P300 component is a positive deflection that occurs approximately 300 ms after the stop signal onset and is associated with activity in the medial frontal cortex (Liotti et al., 2005). The No-Go N200 and N200 in the SSRT task are thought to be the "flag" and associated with processes related to conflict monitoring (Donkers & van Boxtel, 2004; Randall & Smith, 2011). While the P300 has often been used as a marker of attention allocation, Krompinger and colleagues (2010) have suggested that under Go/No-Go and SSRT conditions, it may reflect operation of the "brake" in accordance with Polich's neuroinhibition model of the P3a (Polich, 2007). Therefore, the N200 may reflect conflict monitoring and the subsequent onset of the inhibitory processes and the P300 reflect the success or strength of the inhibitory processes brought to bear. Through the use of the Go/No-Go task and the N200 and P300, Kamijo and colleagues (2012) found that obese children demonstrated different ERP patterns as well as lower response accuracy compared to their healthy weight counterparts. Specifically, they found that obese children had larger No-Go N200 amplitudes relative to the Go N200, but this difference was absent for the healthy weight children. In addition, they found less pronounced No-Go P300 anteriorization in the obese children relative to controls, illustrating that obesity may be negatively and selectively associated with prefrontal inhibitory control.

In an experiment looking at food stimuli specifically, Batterink and colleagues (2010) found that obese individuals, compared to normal weight controls, displayed different patterns of neutral activation when shown food images. A food-specific Go/No-Go task was administered to obese and lean adolescent females during a functional magnetic resonance imaging (fMRI) session. Participants were instructed to respond with a button press to the 'Go' trials, which consisted of images of vegetables, but withhold their responses on the 'No-Go' trials, which consisted of images of desserts, and to respond as quickly and accurately as possible. The results demonstrated that body mass index (BMI) was correlated with response inhibition deficits both behaviorally and neurophysiologically. Specifically, participants with higher BMI scores responded more quickly on the 'Go' trials and made more commission errors on the 'No-Go' trials. They also demonstrated lower activation in the frontal inhibitory regions to the appetizing food images relative to controls. These findings support the relationship between obesity and poor inhibitory control, both at a behavioral and neurophysiological level. However, the issue of counterbalancing was not taken into account. The images were confounded as the 'Go' trials always included images of vegetables, while the 'No-Go' trials always included images of desserts. Therefore, it is difficult to discern whether the obese participants had greater deficits in response to appetizing food. While it is possible to assess both approach and inhibitory behaviors through the Go/No-Go and SSRT task, the SSRT task can be more informative. First, the SSRT task provides an individualized measure of stopping latency as the stop signal appears at varying times to track the individual's progress. Secondly, the SSRT task increases the difficulty of inhibiting the 'Go' response since the 'Stop' signal is presented after the 'Go' and the participant has typically already initiated the 'Go' response by the time the 'Stop' signal is presented. In order to explore specifically how food impacts obese individuals at both the

behavioral and neural level, an ideal experiment would include a food-specific SSRT paradigm with psychophysiological measures, such as ERPs.

The aim of the current study, therefore, was to employ the SSRT task to determine whether inhibitory control in obese subjects was more difficult to achieve in response to food cues relative to other appetitive or neutral stimuli. Inhibitory control in this context is assessed behaviorally by obtaining a measure of stop time and neurophysiologically with event-related brain potentials. During the administration of the SSRT task, obese and normal weight control participants were required to either respond to a stimulus or inhibit that response when a stop signal was presented. The 'Go' and 'Stop' processes are computed to illustrate the amount of time that it took for an individual to respond (Go-RT) and withhold a response (SSRT). The study used three types of stimuli to assess whether obese individuals have greater response inhibition impairment to food cues compared to other cues: food stimuli (e.g. images of high calorie, high fat food), neutral stimuli (e.g. utensils and furniture), and positive stimuli (e.g. babies and animals). Including this positive category allowed for the examination of engaging non-food stimuli in order to assess whether greater inhibitory impairment in obese individuals was specific to food. Both the food and positive stimuli were matched on ratings of valence and arousal; the neutral stimuli were lower on both dimensions.

Consistent with previous findings, it is expected that obese individuals would display a more impulsive response style and respond more quickly than their control counterparts, especially to food stimuli. It is also expected that obese individuals will have more difficulty withholding their responses to all stimuli and display longer SSRTs relative to their control counterparts. In addition, it is anticipated that the obese group will show greater response inhibition impairment to food cues because it is likely to be more difficult to disengage

attentional resources and engage the necessary inhibitory processes in the presence of stimuli that are especially salient and rewarding.

In terms of the ERP components, based on previous studies (Kok, Ramautar, Deruiter, Band, & Ridderinkhof, 2004; Liotti, Pliszka, Perez, Kothmann, & Woldorff, 2005), it is anticipated that the N200 will be larger for unsuccessful trials and lateralized to the right hemisphere. It is also expected that the N200 will be larger for food cues in the obese group reflecting the greater conflict between attentional processing and response inhibition. Consistent with previous findings (Kok et al., 2004; Liotti et al., 2005), it is also predicted that P300 will be larger, peak earlier and show a more frontal distribution when inhibition is successful. In line with the Liotti et al. (2005) finding with ADHD subjects, it is believed that the P300, particularly the P300 associated with successful trials, will be smaller overall in the obese group, as the "brake" mechanism may not be functioning as effectively. Furthermore, it is expected that the P300 for food cues will be even smaller because greater conflict with food may be associated with less effective brakes. These behavioral and ERP results would garner further support for the notion that food is associated with greater response inhibition impairment in obesity.

Chapter 2

METHOD

Participants

Undergraduates in an introductory psychology class at the University of Delaware were asked their height and weight as part of an online pretest measure. By using a BMI formula provided by NIH (Weight in pounds / (Height in inches x Height in inches)) x 703), BMIs were calculated. Students with BMIs above 30 were classified as 'obese' (NIH, 1998; NIH, 2000) and recruited for the study. Likewise, students whose BMIs were classified as 'normal' (BMI = 18.5 to 24.9) were recruited as control subjects. In total, 59 undergraduate students (30 males and 29 females) participated in the study for course credit, of whom 30 were obese subjects and 29 were controls. Group categorizations were confirmed by height and weight measurements taken as part of experimental protocol. Data from three obese participants were excluded from the analyses: one due to equipment malfunction and two because they did not follow instructions.

Stimuli and Procedure

After providing informed consent, participants were brought to a secluded corner to have their height and weight verified. Afterwards, participants were fitted with an electrode cap, seated 0.5 m (as measured to their chest) in front of a computer monitor, and given instructions for both the practice and the experimental trials. Participants completed the task as their EEG was recorded. Visual stimuli were presented on a Pentium I class computer, and Presentation software (Neurobehavioral Systems, Inc.) was used to regulate the presentation and timing of stimuli and to measure reaction times.

Stop Signal Reaction Time (SSRT) Task

Procedure

The SSRT task (Logan et al., 1984) requires the participant to either respond to a stimulus or inhibit that response when a stop signal is presented. On each trial in the present experiment, an image was presented, bordered in green, on either the left or right side. Participants were instructed to press the left or right button of a keypad corresponding to the side on which the border was placed. On 'Stop' trials, a red circle, superimposed on the stimulus, occurred at varying delay intervals. This signaled participants to inhibit their response to the image frame. The three types of images were presented in random order, and the stop signal was randomly presented on approximately a third of the trials. The experiment consisted of 720 total trials. Each participant completed two practice blocks of 50 trials before completing the six blocks of 120 trials that comprised the experiment proper. Participants were instructed to respond as quickly as possible and not to intentionally delay their responses in order to anticipate the 'Stop' signal. They were given feedback after the first practice block and told to speed up their responses if they seemed to be waiting for the 'Stop' signal. After the initial stimulus was presented, the subject had 1000 ms on 'Go' trials and 1200 ms on 'Stop' trials (with a varying delay between the initial stimulus and 'Stop' signal on 'Stop' trials) to respond before the picture disappeared. When a 'Stop' signal appeared, it stayed on for the duration of the trial. Upon removal of the image, the screen was blank for 1000 ms.

Calculation

When the 'Stop' signal occurs soon after the 'Go' signal, it is easier for the participant to inhibit the response and thus, the participant is less likely to fail to inhibit. In contrast, when the 'Stop' signal occurs after a long interval following the 'Go' signal, the participant is more likely

to fail to inhibit (Schachar & Logan, 1990). The SSRT, a measurement of the time needed for the stop processes to reach completion after the 'Stop' signal presentation, can then be calculated. Subtracting out the stop signal delay, which is the delay between the 'Go' stimulus and 'Stop' signal, yields an estimate of reaction time to the 'Stop' signal (see Logan & Cowan, 1984, Schachar & Logan, 1990, and Pliszka et al., 1997 for more details of these procedures). If the 'Go' process finishes first, the participant will respond even though a stop signal was presented, resulting in an Unsuccessful Stop Trial (USST). If the 'Stop' process finishes first, the response is withheld and results in a Successful Stop Trial (SST). Thus, poor inhibitory control is associated with long SSRTs (Logan et al., 1997).

Stimuli

Three types of 'Go' stimuli were approximately equally employed: positive images (e.g., babies and animals), food images (e.g., fast food and candy), and neutral images (e.g., bowls and lamps). The images in this experiment are from a compilation that was previously collected for a food-specific SSRT study in obese children. Specifically, the positive and food images were collected from the Internet while the neutral images were collected from the International Affective Picture System (IAPS) collection (Lang, Bradley & Cuthbert, 2005). Since the positive and food images were not taken from the IAPS set, which collects valence and arousal ratings, a group of students rated the positive and food images on valence and arousal. The positive and food images were roughly equated on valence and arousal ratings, while the neutral images were lower on both.

ERP Recording, Data Reduction, and Analysis

EEG was recorded from 32 Ag/AgCl sintered electrodes embedded in an electrode cap. EEG was digitized at 512 Hz using ANT acquisition hardware (Advanced Neuro Technology,

Enschede, The Netherlands) with an average electrode reference and forehead ground site (AFz). The EEG was re-referenced offline to the average of the two mastoid sites. Continuous EEG was corrected for eye blinks with ASA software from ANT. A bandpass filter from 0.1 Hz to 20 Hz was used. Trials in which an EEG change exceeded a threshold of -75 µV or +75 µV were rejected.

Because the ERPs elicited by stop and go trials overlap, stop signal ERP averages were created after removal of the overlapping 'Go' stimulus ERPs (Kok et al., 2004). That is, difference waves were formed by subtracting the go-ERPs from the stop-ERPs for both successful and unsuccessful trials. The slow go-ERPs were subtracted from the successful stop trials (slow-go results in a successful stop because the stop process terminates before the go process can finish and thus the subject successfully prevents their response) and the fast go-ERPs were subtracted from the unsuccessful stop trials (fast-go results in an unsuccessful stop because the go-process terminates before the stop process can finish and thus, the subject responds to the stop signal). Separate averages were then made for each stimulus type and level of success.

Statistical analyses were conducted in PASW (Version 19.0). Behavioral measures, 'Go' and 'Stop' reaction times and accuracy rate, were evaluated via analysis of variance (ANOVA) for each stimulus type, with BMI group as the between-subject factor. Using General Linear Model software, repeated measures ANOVAs were performed separately for each ERP component with stimulus type (positive, food, and neutral), success (successful and unsuccessful), and laterality/region (right, left for the N200/anterior, posterior for the P300) as within-subject factors. In all analyses, the three stimuli were placed in this order: positive, food, and neutral. Greenhouse-Geisser corrections of degrees of freedom were applied when appropriate. An alpha-level of .05 was defined for all statistical tests.

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RESULTS

Behavioral Results

Table 1   **Average means for GO-RT, SSRT, and stop accuracy rates for both groups**

	Controls	Obese
Positive GO-RT	690	644
Food GO-RT	703	660
Neutral GO-RT	681	640
Positive SSRT	207	227
Food SSRT	212	223
Neutral SSRT	205	215
Positive Stop Accuracy	51	47
Food Stop Accuracy	52	54
Neutral Stop Accuracy	50	50

Note. GO-RT and SSRT (in milliseconds), Stop Accuracy (percentage)

GO-RT

The time it took for participants to respond to 'Go' stimuli was a function of stimulus type in each of the two groups. The analysis revealed a quadratic stimulus effect, as the mean for the food stimuli was slower than the average mean of the positive and neutral stimuli, F_{quad} $(1,54) = 83.821$, $p < .001$. Neither the main effect of Group ($F (1,54) = 1.420$, $p = .239$) nor the Stimulus by Group interaction ($F (2,53) = .639$, $p = .427$) reached statistical significance.

SSRT

SSRT, the behavioral measure of inhibitory control, was not affected by stimulus type. Stimuli were not different from one another (F_{quad} (1,54) = 2.312, p = .134) nor did the stimuli differ by group (F (2,53) = 0.938 p = .337). The hypothesis that obese subjects would take longer to stop than their control counterparts was unsupported (F (1,54) = 1.398, p = .242).

Stop Accuracy Rate

The stop accuracy rate illustrates the success of the adaptive tracking procedures. Controls had an average accuracy rate of 51.06% for stop trials, and obese participants had an average accuracy rate of 50.54% for stop trials. A quadratic stimulus effect was present, indicating that participants were more accurate at stopping on food stimuli than for the average of the other stimuli, F_{quad} (1,54) = 10.732, p = .002. A stimulus by group interaction demonstrated that the obese participants were more accurate at stopping on food trials relative to their control counterparts, F (2,53) = 4.551, p = .037. The between-group difference for accuracy rate did not reach statistical significance, F (1,54) = 1.645, p = .205.
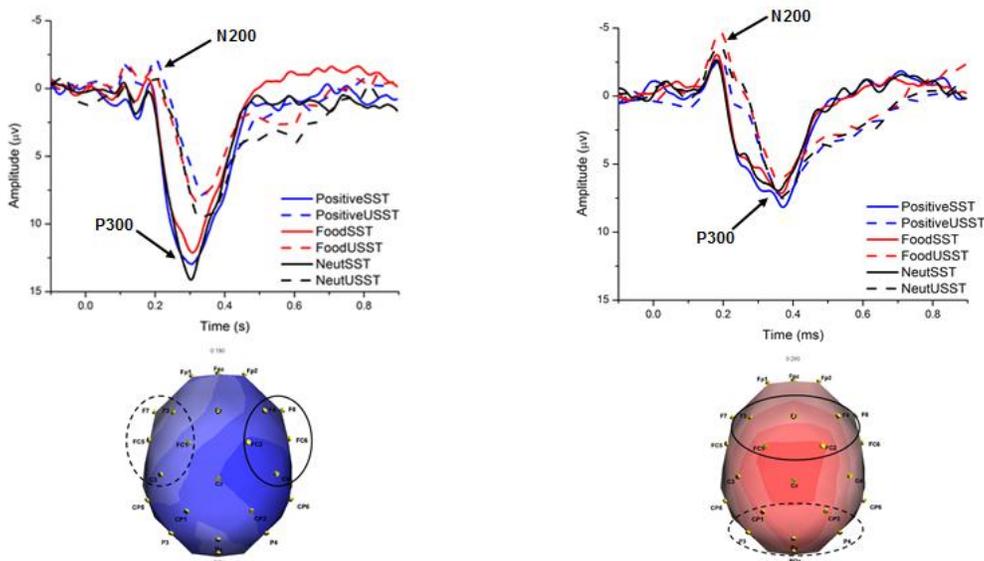
ERP Results

Figure 1   **Grand average ERPs.** The grand average N200 and P300 waveforms for successful and unsuccessful trials with respect to the three different stimuli for both groups. Grand average ERPs for the N200 and P300 components for controls (a) and obese subjects (b), averaged across the anterior ROI. Head plots depict USST for the N200 (left) and SST for the P300 (right), with respective ROIs circled.

N200 Component

The N200 is a negative deflection in the waveform that occurs approximately 200 ms after the presentation of the stop signal. Previous research suggests that the N200 is maximal over the right frontal cortex (Pliszka et al., 2000), and on this basis right and left regions of interest (ROIs) were identified. The right ROI was comprised of the F4, F8, FC2, FC6, and C4 electrodes, and the left ROI was comprised of the F3, F7, FC1, FC5, and C3 electrodes. ROI averages were then used to isolate and quantify the N200 component as the average amplitude within a window from 160 to 210 ms after the stop signal was delivered.

A 3 (Stimulus) by 2 (Success) by 2 (Laterality) by 2 (Group) ANOVA confirmed the lateralization of the N200 with a significantly larger component associated with the right ROI, $F (1,54) = 29.626, p < .001$. The N200 was larger on unsuccessful trials than on successful trials, $F (1,54) = 10.840, p = .002$, and a quadratic stimulus effect ($F_{quad} (1,54) = 9.338, p = .003$) indicated that food trials were associated with the largest N200. There was no overall group difference in N200 amplitude ($F (1,54) = .061, p = .806$), but the analysis did reveal a four way interaction (stimulus x success x laterality x group) such that especially large N200s were prompted in obese subjects when they were unsuccessful in stopping in the presence of the food pictures, $F (2,53) = 8.380, p = .005$.
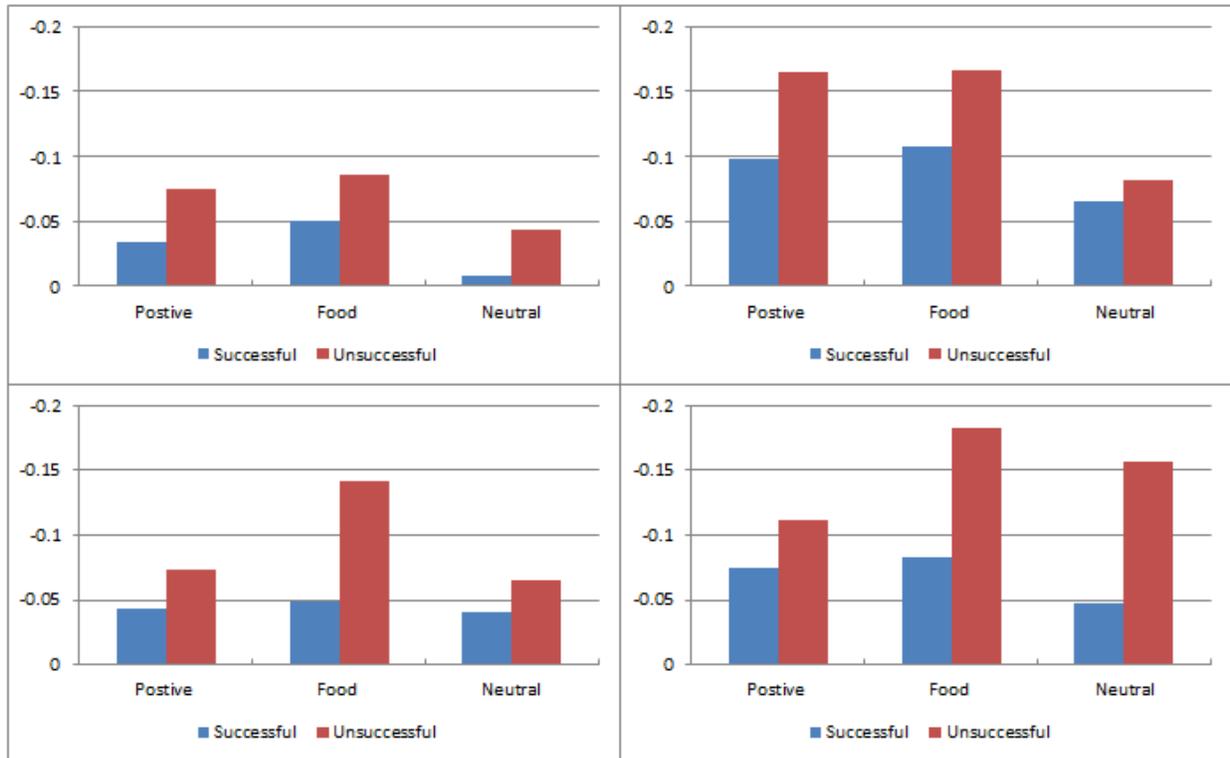
Figure 2   **N200 amplitude.** N200 amplitude for controls and obese subjects across the two left and right ROIs. Controls are depicted in the two top graphs while the obese subjects are depicted in the bottom two graphs.

P300 Component

In the SSRT paradigm, the relevant P300 component is a fronto-central positive deflection that occurs approximately 300 ms after the presentation of the stop signal. Previous research suggests that the P300 arises in the medial frontal cortex (Liotti et al., 2005), and the P300 was quantified after anterior and posterior ROIs were identified. The anterior ROI included the Fz, F3, F4, FC1, and FC2 electrodes and the posterior ROI included the Pz, P3, P4, CP1, and CP2 electrodes. The P300 component was scored as the average amplitude within in the window from 280 to 330 ms after stimulus onset for successful trials and from 335 to 385 ms for unsuccessful trials.

A 3 (Stimulus) by 2 (Success) by 2 (Region) by 2 (Group) ANOVA revealed a highly significant quadratic stimulus effect (F_{quad} (1,54) = 8.375, p = .005), with food trials associated with the smallest P300. Analysis also revealed a Success by Region by Group interaction, indicating that the P300 amplitude was smaller for successful trials in the anterior region for the obese group, F (1,54) = 4.254, p = .044. When looked at as a function of accuracy, there was a group difference only on successful trials; obese subjects displaying a greatly reduced or missing anterior stop P300, F (1,54) = 4.511, p = .038, but the groups did not differ on the more posterior P300 associated with unsuccessful trials (F(1,54) = 0.978, p = .327).
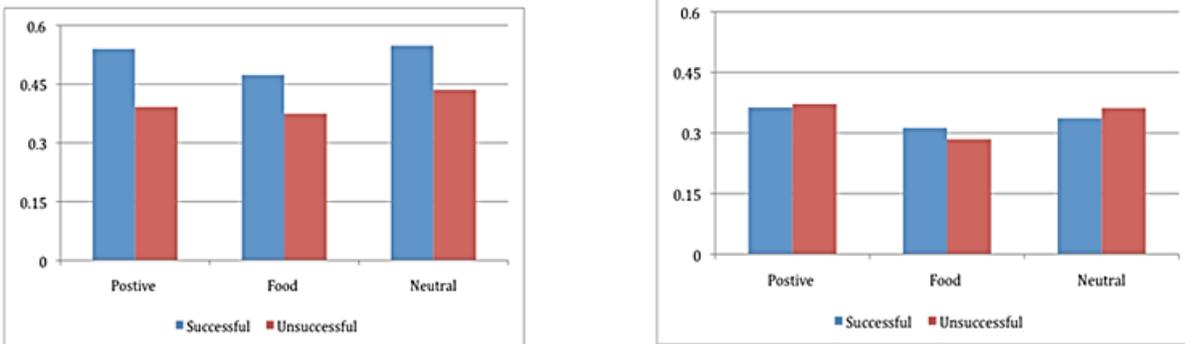

Figure 3   **P300 amplitude.** P300 amplitude at the anterior ROI for controls (a) and obese subjects (b). Stimuli are on the X-axis and P300 amplitude (in microvolt) is on the Y-axis.

Chapter 4

DISCUSSION

The present study investigated the mechanisms of inhibitory control in response to food cues in obese patients. The results of the experiment revealed significant ERP differences mostly nonsignificant behavioral differences between obese individuals and their control counterparts in the absence of significant behavioral differences. Specifically, it took longer for both groups to respond to the food stimuli than to the other stimulus classes and both groups were more accurate at stopping in the presence of food stimuli. Behaviorally, these results suggest that a bias towards food may not be specific to obesity.

In terms of inhibitory control, the SSRT, a behavioral measure of inhibition, did not significantly differ between the two groups. Although this was inconsistent with our initial hypotheses, SSRT results in comparisons involving obese and normal-weight subjects have been largely inconsistent in the existing literature (Braet & Crombez, 2003; Loeber et al., 2012; Soetens & Braet, 2007). Stronger evidence of abnormal inhibitory control in obese subjects was found in two ERP components. The N200 was larger for food cues, specifically on the unsuccessful trials in the obese group, whereas food stimuli were generally associated with smaller P300s in both groups. Most striking in the P300 data was the difference between successful and unsuccessful trials and the virtual absence of the stop signal P300 in the group of obese subjects. Together, the behavioral and ERP findings suggest that food affects the cognitive processes associated with attending to and inhibiting in both obese individuals and their control counterparts, but obese individuals appear to be further affected when needing to inhibit their responses more generally. These results somewhat support the impaired response inhibition and salience attribution model, which proposes that addiction, or in this case obesity,

is characterized by increased saliency to reward stimuli and also by inhibitory control deficits. However, these results illustrate that in the obesity specific impaired response inhibition and salience attribution model, the increased saliency to reward stimuli is not restricted to food.

Focusing specifically on the ERP components and the "flag" and "brake" model, if the N200 and P300 represent the flag and brake respectively, the findings illustrate a functioning yet hypersensitive "flag" but problematic "brake" in obese individuals. It had been hypothesized that the N200 would be larger in the obese group for food trials, compared to positive and neutral trials. Larger N200 were found for food trials, which suggests that obese individuals are more susceptible to food as food cues were associated with more conflict on these trials. This indicates that food images may require additional cognitive resources during the execution of the stop process in obese individuals and, unlike the behavioral data, suggests a subtle bias in obese subjects specific to food-related stimuli. It was also expected to find smaller P300 for food trials in the obese group; however, the P300 for food trials were smaller in both groups. This did not translate into longer stop times when food stimuli were present, however. The most striking feature of the P300 was the overall amplitude reduction in the obese group suggesting that a weaker "brake" was applied. As this was not associated with significant behavioral sequelae, it may be that a different inhibitory network may be operating in obesity.

Kamijo and colleagues (2012) demonstrated similar P300 findings showing that obese children had smaller P300 to no-go trials compared to healthy weight children. Likewise, in ADHD, another inhibitory control disorder, Liotti and colleagues (2005) reported a marked reduction in P300 amplitude for successful inhibitions in ADHD children. They stated that the larger P300 for successful inhibitions reflected the more efficient monitoring or successful implementation of the response inhibition process and suggested that the reduction in amplitude

likely represented a deficit in in this process. It is possible that the lack of successful and

unsuccessful trial differentiation for obese individuals reflects inferior inhibitory control and

possibly a difference in the prefrontal cortex of obese individuals (Batterink, Yokum, & Stice,

2010; Davids et al., 2009). Hendrick and colleagues' (2011) findings also support the results of

the current study, as they also reported nonsignificant differences between groups on the SSRT

task, but demonstrated that the two groups had differences in brain activation to stop trials. It is

plausible that lower activation in inhibitory regions in obese individuals during stop trials may be

associated with the diminished successful P300s and that alternative mechanisms of inhibitory

control may be employed by such subjects.

It is possible that the flag and brake model as articulated by Krompinger and colleagues

(2010) is incorrect in that P300 may not be related to a braking mechanism. An argument

against the P300 representing the brake is that a few studies have shown P300 differences and

nonsignificant SSRT results. Therefore, if the brake were to be malfunctioning in obese

individuals, their SSRTs should be significantly slower. However, they are not. Rather than

reflecting the successful implementation of the inhibitory processes, it is possible that the P300 is

reflecting response monitoring, the ability to monitor one's responses. Skoranski and colleagues

(2013) examined whether obese children differed from controls in their response monitoring and

found that obese children demonstrated smaller error-related negativity (ERN), an ERP

component associated with response monitoring. Therefore, the smaller P300 in the obese group

may not be indexing the strength of the stop, but rather reflecting their monitoring, similar to the

smaller ERN in the obese children. Furthermore, the SSRTs occur almost a 100ms before the

P300, which is also a challenge to the idea that the P300 characterizes the functioning of the

brake. Though the P300 has not been previously thought of as a marker of response monitoring,

it may be worthwhile for future studies to further investigate the role of the P300 in inhibitory

control in obesity.

There are several limitations of the study that should be noted at this point. First, ratings

of valence and arousal were based on similar content pictures from the IAPS collection (Lang,

Bradley, & Cuthbert, 2005) and were not normed independently. Also, in the current

experiment, only the neutral pictures were drawn for the standard IAPS picture set. Although the

IAPS contains pictures similar to those contained in our positive and food categories, they are

not identical and would need to be standardized along with the neutral pictures before any future

applications. It would be particularly important to have each participant rate the hedonic valence

and emotion behind the images to assess whether certain images are more appealing to certain

individuals. Another limitation was the way BMI was calculated. It was determined whether an

individual was normal or obese by calculating the individual's height and weight, but it did not

account for muscle composition. Therefore, this sample of participants may have been

heterogeneous, as some participants may have been considered obese due to muscle mass and

not fat content. An individual who is considered obese due to large muscle mass may have

cognitive or neural differences from an individual who is considered obese due to high fat

content. Thus, future studies should add extra measures, such as the use of a skinfold test, which

determines subcutaneous fat, or waist circumference in relation to height.

Overall, the present study provides further insight into the negative association between

obesity and inhibitory control using behavioral and electrophysiological measures of response

inhibition. As has been shown, obesity is associated with an atypical P300 pattern. Obese

individuals displayed similar N200s to controls but their P300s, specifically the successful stop

P300s, were reduced relative to controls, though no significant behavioral differences between

groups were found. The current findings suggest that inhibitory control deficiencies in obesity

may stem from abnormal cognitive processes and either alternative mechanisms or behavioral

compensatory strategies have been developed, which may explain the absence of behavioral

differences between the two groups. These results also add to the body of literature illustrating

that a specific inhibitory deficit to food is not at the core of obesity, rather a general inhibitory

deficit.

REFERENCES

Barch, D. M., Braver, T. S., Carter, C. S., Poldrack, R. A., & Robbins, T. W. (2009). CNTRICS final task selection: Executive control. *Schizophrenia Bulletin, 35*, 115–135.

Braet, C., & Crombez, G. (2003). Cognitive interference due to food cues in childhood obesity. *Journal of Clinical Child and Adolescent Psychology*, *32*, 32–39.

Batterink, L., Yokum, S., & Stice, E. (2010). Body mass correlates inversely with inhibitory control in response to food among adolescent girls: an fMRI study. *Neuroimage*, *52*, 1696–1703.

Berridge, K. C. (2007). Brain reward systems for food incentives and hedonics in normal appetite and eating disorders. In Kirkham, T. C., & Cooper, S. J. (Eds.), *Progress in Brain Research: Appetite and Body Weight* (pp. 191–216). New York, NY: Academic Press.

Chalmers, D. K., Bowyer, C. A., & Olenick, N. L. (1990). Problem drinking and obesity: A comparison in personality patterns and life-style. *International Journal of the Addictions*, *25*, 803–817.

Davids, S., Lauffer, H., Thoms, K., Jagdhun, M., Hirschfeld, H., Domin, M., …Lotze, M. (2009). Increased dorsolateral prefrontal cortex activation in obese children during observation of food stimuli. *International Journal of Obesity*, *34*, 94–104.

DeJong, R., Coles, M. H., Logan, G. D., & Gratton, G. (1990). In search of the point of no return: the control of response processes. *Journal of Experimental Psychology: Human Perception and Performance, 16*, 164–182.

Donkers, F. C., & van Boxtel, G. J. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. *Brain and cognition*, *56*, 165–176.

Epstein, L. J., Temple, J. L., Neaderhiser, B. J., Salis, R. J., Erbe, R. W., & Leddy, J. J. (2007). Food reinforcement, the dopamine D2 receptor genotype, and energy intake in obese and nonobese humans. *Behavioral Neuroscience*, *121*, 877–886.

Goldstein, R. Z., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry*, *159*, 1642–1652.

Hendrick, O. M., Luo, X., Zhang, S., & Li, C.-s R. (2011). Saliency processing and obesity: A preliminary imaging study of the stop signal task. *Obesity*. doi:10.1038/oby.2011.180.

Kamijo, K., Pontifex, M. B., Khan, N. A., Raine, L. B., Scudder, M. R., Drollette, E. S., …Hillman, C. H. (2012). The association of childhood obesity to neuroelectric indices of inhibition. *Psychophysiology*, *49*, 1361–1371.

Kok, A., Ramautar, J. R., Deruiter, M. B., Band, G. H., & Ridderinkhof, K. R. (2004). ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology*, *41*, 9–20.

Krompinger, J. W., Janes, J., Chernow, K., Henderson, R., & Simons, R. F. (2010, September). The effect of depression on your cognitive brakes: Evidence from event-related potentials. Poster presented at the 49th Annual Meeting of the Society for Psychophysiological Research, Portland, OR.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2005). International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-6. University of Florida, Gainesville, FL.

Liotti, M., Pliszka, S. R., Perez, R., Kothmann, D., & Woldorff, M. G. (2005). Abnormal brain activity related to performance monitoring and error detection in children with ADHD. *Cortex, 41*, 377–388.

Loeber, S., Grosshans, M., Korucuoglu, O., Vollmert, C., Vollstadt-Klein, S., Schneider, S., …Kiefer, F. (2012). Impairment of inhibitory control in response to food-associated cues and attentional bias of obese participants and normal- weight controls. *International Journal of Obesity*, *36*, 1334–1339.

Logan, G. D. & Cowan, W. B. (1984). On the ability to inhibit thought and action: a theory of an act of control. *Psychological Review*, 91(3): 295–327.

Logan, G. D., Cowan, W. B., & Davis, K. A. (1984). On the ability to inhibit simple and choice reaction time responses: a model and a method. *Journal of Experimental Psychology: Human Perception and Performance*, *10*, 276–291.

Logan, G. D., Schachar, R. J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science, 8,* 60–64.

National Institutes of Health, National Heart, Lung, and Blood Institute (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obesity Research*, *6*, S51–210.

National Institutes of Health (2000). The Practical Guide to the Identification, Evaluation and Treatment of Overweight and Obesity in Adults. Bethesda, MD: U.S. National Institutes of Health.

Nederkoorn, C., Braet, C., Van Eijs, Y., Tanghe, A., & Jansen, A. (2006a). Why obese children cannot resist food: The role of impulsivity. *Eating Behaviors, 7*, 315–322.

Nederkoorn, C., Jansen, E., Mulkens, S., & Jansen, A. (2007). Impulsivity predicts treatment outcome in obese children. *Behaviour Research and Therapy, 45*, 1071–1075.

Nederkoorn, C., Smulders, F. T. Y., Havermans, R. C., Roefs, A., & Jansen, A. (2006b). Impulsivity in obese women. *Appetite, 47*, 253–256.

Pliszka, S. R., Borcherding, S. H., Spratley, K., Leon, S., & Irick, S. (1997). Measuring inhibitory control in children. *Journal of Developmental & Behavioral Pediatrics*, *18*, 254–259.

Pliszka, S. R., Liotti, M., & Woldorff, M. G. (2000). Inhibitory control in children with attention-deficit/hyperactivity disorder: Event-related potentials identify the processing component and timing of an impaired right-frontal response-inhibition mechanism. *Biological Psychiatry, 48*, 238–246.

Polich, J (2007). Updating P300: an integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*, 2128–2148.

Randall, W. M., & Smith, J. L. (2011). Conflict and inhibition in the cued-Go/NoGo task. *Clinical Neurophysiology*, *122*, 2400–2407.

Rydén, A., Sullivan, M., Torgerson, J. S., Karlsson, J., Lindroos, A.-K., & Taft, C. (2003). Severe obesity and personality: A comparative controlled study of personality traits. *International Journal of Obesity*, *27*, 1534–1540.

Saelens, B. E., & Epstein, L. H. (1996). Reinforcing value of food in obese and non-obese women. *Appetite*, *27*, 41–50.

Schachar, R., & Logan, G. D. (1990). Impulsivity and inhibitory control in normal development and childhood psychopathology. *Developmental Psychology*, *26*, 710–720.

Skoranski, A. M., Most, S. B., Lutz-Stehl, M., Hoffman, J. E., Hassink, S., & Simons, R. F. (2013). Response monitoring and cognitive control in childhood obesity. *Biological Psychology*, *92*, 199–204.

Soetens, B., & Braet, C. (2007). Information processing of food cues in overweight and normal weight adolescents. *British Journal of Health Psychology*, *12*, 285–304.

Volkow, N. D., & Wise, R. A. (2005). How can drug addiction help us understand obesity? *Nature Neuroscience*, *8*, 555–560.

Wang, G.-J., Volkow, N. D., Logan, J., Pappas, N. R., Wong, C. T., Zhu, W.,…Fowler, J. S. (2001). Brain dopamine and obesity. *Lancet*, *357*, 354–357.

Appendix

IRB APPROVAL LETTER AND DOCUMENTATION

DATE: June 16, 2011

TO: Steven Most, Ph.D.
FROM: University of Delaware IRB

STUDY TITLE: [162063-4] Neuro-cognitive mechanisms of self-regulation and their relation to childhood obesity

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: June 15, 2011

EFFECTIVE DATE: June 16, 2011
EXPIRATION DATE: June 16, 2012
REVIEW TYPE: Full Committee Review

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that <u>informed consent</u> is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Generated on IRBNet

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Jody-Lynn Berg at (302) 831-1119 or jlberg@udel.edu. Please include your study title and reference number in all correspondence with this office.