From outcomes to actions: Fundamental mechanisms in reward seeking
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External stimulus control over action for food in obese versus lean individuals

A version of this chapter has been submitted as: Watson, P., Wiers, R. W., Hommel, B., Gerdes, V.E.A., & de Wit, S. (submitted). External stimulus control over action for food in obese versus lean individuals.
Abstract

Background/Objectives: Our obesogenic environment is considered a significant contributor to the obesity epidemic. In the current study we examined a mechanism by which food cues (signaling low- versus high-calorie food) can bias instrumental responses directed towards those foods. To investigate the clinical relevance of this mechanism, we used a computerized associative learning task and compared performance of a group of severely obese individuals to that of a healthy-weight control group.

Subjects/Methods: Performance of 19 severely obese individuals was compared to 19 healthy-weight controls matched for age, education and gender. During a response-priming test we exposed participants to both food pictures and to Pavlovian cues predictive of those food pictures, and examined their biasing effect on instrumental choice. We expected priming to be stronger with palatable, high-calorie foods (potato chips and chocolate) relative to low-calorie foods (lettuce and zucchini) and, furthermore, that this interaction would be particularly pronounced in obese individuals.

Results: Statistical analysis revealed an interaction between calorie and group, $F(1,36)=6.9$, $MSE=0.08$, $p=0.01$. When collapsing across cue type (food picture or Pavlovian cue) obese participants showed higher priming rates for the high-calorie versus the low-calorie outcomes, $t(18)=3.1$, $p=0.006$, 95% CI [6%, 33%]. By contrast, in the healthy-weight group, performance between the high and low-calorie outcomes did not differ, $t(18)=0.58$, $p=0.57$, 95% CI [-16%, 9%].

Conclusions: As predicted, obese individuals are particularly vulnerable to the biasing effects of high- relative to low-calorie food cues.
1. Introduction

Obesity is a major public health issue and is becoming increasingly prevalent (OECD, 2014). The causes are multi-faceted, but our obesogenic environment with cues signaling tasty, palatable food, is argued to play a significant role (Cohen, 2008; Johnson, 2013; Swinburn et al., 2011). Scientific evidence that food-associated cues detrimentally influence food choice can inform efforts to regulate the food industry (Harris, Pomeranz, Lobstein, & Brownell, 2009). In the current study we examined an associative mechanism by which food-associated cues (both low and high calorie) can bias instrumental responses directed towards those foods. To investigate the clinical relevance of this mechanism, we compared the performance of a group of severely obese individuals to that of healthy-weight controls in a computerized associative learning task.

A number of previous studies have assessed the effect of food triggers on behavior in carefully controlled laboratory settings. For example, presentation of pictures of chocolate on a computer screen will elicit key presses that have previously yielded this food reward (Hogarth, 2012; Hogarth & Chase, 2011). In fact, merely showing an abstract picture previously associated with chocolate will have this biasing effect on choice (Bray et al., 2008; Lovibond & Colagiuri, 2013; Prévost et al., 2012; Watson et al., 2014). Figure 1 depicts these two types of response priming: direct outcome-response (O-R) priming (captured for example by ideomotor theory; Hommel, 2009; Hommel et al., 2001); and indirect stimulus-outcome-response (S-O-R) priming (also known as Pavlovian-to-instrumental transfer, PIT, see for review: S. de Wit & Dickinson, 2009). We have previously argued that these associative response-priming mechanisms enable the obesogenic environment to trigger maladaptive...
food-seeking behavior, ultimately contributing to overeating and obesity (Swinburn et al., 2011; Watson et al., 2014). To substantiate this claim, the present study investigates whether this mechanism is particularly potent in obese individuals.

Figure 1: A) Direct (O-R) Priming – the sight of a croissant triggers a trip to the bakery B) Indirect response priming – seeing a painting of Paris reminds one of croissants, triggering a trip to the bakery.

In the current study we used an associative learning task (Watson, Wiers, Hommel, Ridderinkhof, & de Wit, 2016) to investigate whether choice behavior of severely obese individuals is vulnerable to the effect of external reminders of palatable, high-calorie food rewards, than that of healthy-
weight controls. As unhealthy food choices are thought to be an important contributor to obesity (World Health Organization, 2015), we compared high- and low-calorie food outcomes. During an initial instrumental training phase, participants earned food pictures (and points) by pushing specific keyboard keys. For example, a left key press led to a picture of chocolate and a right key press to a picture of lettuce (Figure 2, top panel). Subsequently, during Pavlovian training, participants learned the relationships between abstract logos and these same food pictures (Figure 2, bottom panel). Finally, in a response-priming test, participants were shown the logos and food pictures and for each image they had to quickly and spontaneously select a key. We measured the extent to which instrumental responses would be primed both directly (by the food pictures) and indirectly (by the Pavlovian logos previously associated with the food pictures). We expected that the palatable, high-calorie food pictures would more readily prime the associated instrumental responses than low-calorie food, and that this effect would be stronger in the obese individuals relative to the healthy-weight controls.

We also included a slips-of-action test (SOAT; S. de Wit et al., 2012; Gillan et al., 2011) to investigate whether participants would be able to flexibly inhibit previously learned responses based on instructed devaluation of the outcomes or whether they would commit habitual “slips of action”. Related tasks have previously been used to show that patients with obsessive-compulsive disorder, alcohol addiction, binge-eating disorder (BED) and obesity are generally less flexible in their behavior (Coppin, Nolan-Poupart, Jones-Gotman, & Small, 2014; Zhang, Manson, Schiller, & Levy, 2014) and more prone to relying on habits (Gillan et al., 2011; Horstmann et al., 2015; Sjoerds et al., 2013; Voon et al., 2015). We expected that obese individuals
would make more slips of action compared to healthy-weight controls, particularly for responses directed towards high-calorie food.

Finally, to investigate the relationship between impulsivity, obesity, and cue-elicited response priming, we included a self-report measure (the Barratt’s Impulsivity Scale) and a Stop Signal Reaction Time (SSRT) task. Obese individuals are reportedly relatively impulsive – scoring high on both self-report measures (Mobbs, Crépin, Thiéry, Golay, & Van der Linden, 2010; Terracciano et al., 2009) and response inhibition tasks (Nederkoorn, Braet et al., 2006; Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006; see review: Schag, Schönleber, Teufel, Zipfel, & Giel, 2013). In line with this, individuals with high trait impulsivity are argued to be more sensitive to reward-associated cues (Carver & White, 1994; Muhle-Karbe & Krebs, 2012; Stanford et al., 2009).

In summary, the aims of the current study were to assess whether choice behavior of obese individuals is more sensitive to the biasing effect of food-associated cues, particularly in the context of palatable, high-calorie food. Both direct (O-R) and indirect (S-O-R) forms of response priming were examined and were related to individual differences in performance on the SOAT and impulsivity.

2. Methods

Participants. Following approval by the University of Amsterdam Psychology Ethics Committee, patients who were in the process of preparing for bariatric surgery to reduce their BMI were recruited from a local hospital (MC Slotervaart). None of the invited patients had been assessed by the psychologist and dietician of the bariatric surgery team as meeting the DSM
criteria for BED. Researchers did not have access to medical records but approached individuals in the waiting room and asked if they would like to take part in a 90-min study investigating memory. Payment of €15 was offered. 28 obese individuals were subsequently tested. Participants who reported having an axis 1 disorder and/or who were taking psychoactive medication were subsequently excluded. The only exception to this was a diagnosis of depression and use of SSRIs (selective serotonin se-uptake inhibitors), which were considered to be acceptable for inclusion. In total, nine patients were eventually excluded from the obese group - one was subsequently found to not be a patient (was attending the clinic with a friend), one individual was post rather than pre-operative, one participant had been treated in the past two years for cocaine addiction and was taking multiple psychoactive drugs, one participant reported having short-term memory loss after an accident, one participant had a diagnosis of ADD and took Ritalin, one participant had learning disabilities, one participant was being treated for alcohol addiction at the time of testing, one participant had a mood-disorder diagnosis and one participant was prescribed with a mood-stabilizing drug. Of the 19 obese participants that remained, four had previously been diagnosed with depression and were taking SSRIs. Using the same cover story of a study investigating memory, control participants were concurrently recruited from two sources – 23 participants from the University of Amsterdam student population (recruited via testuva.nl) to fulfill testing obligations for a student project and 25 participants from the community (recruited via proefbunny.nl and digiprik.nl) to fulfill demographic requirements. Participants who registered their interest were asked to fill in a short demographic questionnaire before being invited for testing. From the student sample (23 datasets), data from four participants was used in the final analysis (chosen on the basis of demographic
information without reference to performance data). Of the 19 remaining datasets, three were discarded because actual BMI was found to be higher than had been reported (>25 kg/m2) and data from 16 participants was not used due to the high levels of education and low age of this sample. Of the community sample (25 datasets), five datasets were discarded due to high BMI (>25 kg/m2) and five datasets were not used on the basis of demographic mismatch with the final obese group. Statistical analysis only commenced once exclusions had been made. Detailed demographic information of the 19 obese individuals and 19 gender, age and education-matched controls can be found in Table 1.

The analysis was repeated with inclusion of all 40 healthy-weight control-group participants and is detailed in the results section.
<table>
<thead>
<tr>
<th></th>
<th>Obese group</th>
<th>Control group</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group size (n)</td>
<td>19</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Gender Ratio M:F</td>
<td>2:17</td>
<td>2:17</td>
<td>Equal ratio</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>43.8y (10.9y)</td>
<td>45.0y (14.0y)</td>
<td>t(35)=0.3, p=0.78</td>
</tr>
<tr>
<td>BMI (SD)</td>
<td>44.3 (7.1)</td>
<td>23.0 (1.6)</td>
<td>t(35)=12.8, p&lt;0.0001</td>
</tr>
<tr>
<td>Education Ratio</td>
<td>3:10:6</td>
<td>3:8:8</td>
<td>χ² (2, n = 19)=1.0, p=0.59 n.b. some cells have less than 5 entries.</td>
</tr>
<tr>
<td>High School: Vocational College: University</td>
<td>62(9)</td>
<td>61 (12)</td>
<td>t(35)=1.9, p=0.83</td>
</tr>
<tr>
<td>BIS total score (SD)</td>
<td>62(9)</td>
<td>61 (12)</td>
<td></td>
</tr>
<tr>
<td>SSRT (SD)</td>
<td>254ms (45ms)</td>
<td>268ms (108ms)</td>
<td>t(35)=0.5, p=0.61</td>
</tr>
<tr>
<td>DBEQ External Eating (SD)</td>
<td>3.2 (0.4)</td>
<td>2.8 (0.6)</td>
<td>t(35)=2.3, p=0.03</td>
</tr>
<tr>
<td>Pre-test Hunger Rating (SD)</td>
<td>22% (24%)</td>
<td>30% (29%)</td>
<td>t(35)=0.9, p=0.36</td>
</tr>
<tr>
<td>Pre-test Desire for high calorie (SD)</td>
<td>46% (30%)</td>
<td>28%(25%)</td>
<td>t(35)=1.9, p=0.06</td>
</tr>
<tr>
<td>Pre-test Desire of Low calorie (SD)</td>
<td>24% (20%)</td>
<td>26% (21%)</td>
<td>t(35)=0.3, p=0.81</td>
</tr>
<tr>
<td>Pre-test Stress Rating (SD)</td>
<td>35% (26%)</td>
<td>20%(22%)</td>
<td>t(35)=1.9, p=0.05</td>
</tr>
</tbody>
</table>

*Table 1: Demographics of the sample. BIS = Barratt Impulsivity Scale; SSRT = Stop Signal Reaction Time; AUDIT = Alcohol Use Disorder Identification Test; DBEQ = Dutch Behavioral Eating Questionnaire.*
**Stimuli and materials.** The computerized response-priming task used was as outlined by Watson and colleagues (2014) - but with different images and cover story. The SOAT was based on that of de Wit and colleagues (2012). The tasks are described in the Procedure (see also Figures 2 and 3). Four black-and-white logos functioned as discriminative cues and another four logos functioned as Pavlovian cues (200 x 200 pixels). Photographs measuring 260 x 160 pixels of potato chips, chocolate, lettuce and zucchini functioned as outcomes (see Figure 2).

**Food Desire, Hunger and Stress Questionnaire.** Participants were asked to rate their hunger, stress, and desire for each food on 10-cm VAS scales marked with the anchors: “none”, “neutral” and “very much”.

**Questionnaires.** Eating motivations were assessed with the external eating subscale of the Dutch Eating Behavioral Questionnaire (DEBQ; van Strien, Frijters, Bergers, & Defares, 1986). The Barratt Impulsivity Scale (BIS-11; Patton, Stanford, & Barratt, 1995) was used to measure impulsivity.

**SSRT.** Response inhibition was measured with the SSRT (Logan et al., 1997). Our version contained four blocks of 64 trials. A staircase-tracking procedure ensured that participants were able to inhibit on approximately 50% of trials. Following successful stopping the stop signal delay was increased by 50ms, whereas following unsuccessful stopping the delay was decreased by 50ms. Longer SSRTs indicate greater difficulty in inhibiting prepotent responses.

**Procedure.** Participants were tested on a laptop. Obese participants were tested in a room at the hospital and control group participants were tested
either at the University, or at their home (only if individuals could be tested alone, without distraction). Participants were first given a potato chip and small pieces of chocolate, lettuce and raw zucchini. They then tasted each and completed the food desire, hunger and stress questionnaire.

They were then given instructions for the “Delicious Snack Game” in which they were told as a cover story that they were driving along the motorway and they had to earn points by collecting as many items of food as possible from various food stores along the way. Two cinema passes for the three highest performers was offered as incentive. For all stages of the task described below, the experimenter showed the participants example trials from a booklet (with different logos and food pictures) and confirmed that the instructions were clear before continuing.
Figure 2: **Response-priming task design.** Participants first learned the relationship between instrumental responses and food pictures (zucchini, lettuce, chocolate and potato chips). They then learned the relationships between four Pavlovian logos and these same food pictures. Direct response priming occurs if presentation of the food pictures during the test phase triggers the previously associated response (e.g. chocolate → left key). Indirect response priming is observed if the Pavlovian logo triggers the response associated with the signaled food picture (e.g. Square logo → chocolate → left key).
The task began with the instrumental training phase. Different logos signaled to participants that a particular food was available and that a left or right key press was required to obtain it. Participants learned by trial and error which key press would be rewarded in the presence of each of the four discriminative logos. Correct responses were followed by a picture of the food outcome, a cash register sound and one point was added to their total score (displayed on screen). Incorrect responses were followed by a buzzer sound and “0”. “Too late” was displayed if no response was recorded within 2s. Feedback was displayed for 1s. Across participants, each of the food pictures was paired with each of the Pavlovian logos (using permutation) and was paired equally often with the left or right key. For each participant, the two response keys were each paired with one high-calorie and one low-calorie food picture. 80 trials contained ten blocks in which the four logos were randomly presented twice.

During the Pavlovian training phase participants first passively viewed the screen and were asked to remember the relationships between four new logos and the same four foods (see Figure 2). For 3s a (Pavlovian) logo was presented at the top of screen - for the final second one of the four food pictures appeared underneath the logo. The relationships between the logos and the food pictures were permuted across participants. After 8 trials (two random presentations of the four logo-food combinations) participants were told that they would be tested on what they had just learned. On each trial of active Pavlovian training a logo was presented at the top of the screen and smaller versions of the four food pictures presented underneath in a random 2x2 matrix. Participants had 3s to click on the correct food image with the mouse. Feedback (1s) was the full-size image of the correct food picture with either the number of points
displayed above (“1” or “0” for correct or incorrect responses) or “too late” for response omissions. 80 trials contained ten blocks in which the four logos were randomly presented twice.

On each trial of the response-priming test a logo or food picture was presented. Participants were instructed to select either the left or the right key as quickly as possible in order to collect the signaled food. If they weren’t sure they were told to not think too hard about the correct response but to spontaneously select a key in a non-systematic order. They would not receive any feedback on their responses but were still earning points. On each trial one of the twelve pictures that had been used in the task was presented for 2s or until a response was made (the four food pictures to assess direct priming, the four Pavlovian logo stimuli to assess indirect response priming and the four instrumental logo stimuli as a control condition). No feedback was given. 48 trials contained 2 blocks in which the 12 pictures were randomly presented twice. The ITI during the response-priming task was 1-2s (random).

Participants then had a 5-minute break before continuing with the SOAT. This began with four refresher blocks of instrumental training (32 trials). Participants were then tested on their knowledge of the O-R relationships during a brief outcome-devaluation test (S. de Wit et al., 2007). On each trial, two of the outcome pictures (either both low-calorie or both high-calorie) were presented for 2s, one above the other (see Figure 3). Participants had to press the key belonging to the still-valuable food outcome that did not have a red cross through it. No feedback was given. During 8 trials each outcome was devalued four times. Finally, participants performed the SOAT. Participants were instructed that they should not
respond for devalued foods (those with a red cross through them). At the start of each of four blocks, the food outcomes were presented on screen, but two of these (one high and one low calorie) had a red cross through them to indicate that these would now lead to subtraction of points. Subsequently, a series of discriminative logos were presented for 1s. Participants were instructed to earn points by pressing the appropriate keys for logos associated to still-valuable outcomes (“go trials”) but to refrain from responding for logos associated with a now-devalued food item (“no-go” trials). No feedback was given. Each of the four logos was shown four times per block, and across blocks, each of the outcomes was devalued twice. We also administered a baseline version of the task that was identical except that participants now saw the four logos appear at the start of each block. This baseline version places similar demands on working memory/response inhibition, but unlike the slips-of-action test it does not require evaluation of an anticipated outcome. The order of the two tests was counterbalanced across participants.

Participants then completed the SSRT task, BIS and DEBQ questionnaires. Weight and height were measured and payment given.
Figure 3: *Slips-of-action task design*. Participants first repeated the instrumental training phase. In the outcome-devaluation test they then had to select the key that led to the still-valuable outcome (no red cross). Finally they had to memorize which food outcomes were still valuable and then decide upon presentation of every logo whether or not they should respond for the outcome it signaled.
**Statistics:** Accuracy and RT (correct trials only) were subjected to separate ANOVAs with group (obese/healthy weight); calorie (high/low); and for the training phases, block (1-10) as variables. Greenhouse-Geisser p values are reported with the original degrees of freedom. A significance criterion of \( p=0.05 \) was adopted and all reported t-tests were two-tailed. Marginally significant results (0.05<\( p <0.10 \)) will be reported upon but not investigated further.

3. Results

**Participants.** As can be seen in Table 1, the groups were matched on gender, age and education level. While there were no significant differences between the groups on pre-test hunger rating or desire for the low-calorie foods, the obese group did report higher levels of desire for the high-calorie foods. Contrary to expectations, the groups did not differ significantly on the BIS total score or SSRT. The obese group, however, scored significantly higher on DBEQ external eating, and reported higher levels of stress.

**Instrumental Training Phase.** Participants had learned by the end of instrumental training which key press was required to successfully obtain food pictures with mean accuracy of 86\% (SD:20\%) during the final block. Showing performance improvement over time, the accuracy analysis revealed a main effect of block, \( F(9,315)=15.5, MSE=0.09, p<0.0001 \). There were no further significant results (all ps>0.28).

The RT analysis revealed a main effect of block only, \( F(9,171)=4.8, MSE=181096, p=0.03 \), indicating that participants became faster over the course of training. There were no further significant results (all ps>0.27).
**Pavlovian Training Phase.** The accuracy analysis confirmed that participants became more accurate over the course of Pavlovian training at associating particular logos with food outcomes, as indicated by a main effect of block, $F(9,279)=5.4$, $MSE=0.05$, $p<0.0001$ (see figure 4). There were no further significant results (all $p$s>0.33). Likewise, for the RT analysis there was a main effect of block only, $F(9,216)=14.2$, $MSE=15837$, $p<0.0001$. There were no further significant results (all $p$s>0.14).

![Figure 4: Training Phases](image)

**Test Phase – Direct & Indirect Response Priming.** Participants demonstrated that the discriminative associations from the instrumental training phase were still present with mean accuracy of 73% (SD:23%) on trials in which the discriminative stimuli were presented. The data of interest were response-priming rates on trials where either the food pictures (direct response priming) or Pavlovian logos (indirect response priming) were presented. Trials were considered accurate (and priming successful) when participants selected the response that during
O-R priming in obesity

instrumental training had yielded the outcome currently being presented/signaled. The mean priming rate was 60%, significantly higher than 50% chance level, $t(37)=3.7, p=0.001$. To compare the effect of calorie on both direct and indirect priming, cue type was added to the ANOVA. This analysis revealed an interaction between calorie and group, $F(1,36)=6.9$, $MSE=0.08$, $p=0.01$, but no significant effects involving cue type (all $p$s>0.17). As can be seen in Figure 5, when collapsing across cue type, obese participants showed higher priming rates for the high-calorie versus the low-calorie outcomes, $t(18)=3.1, p=0.006$, 95% CI [6%, 33%]. In fact, low-calorie priming rates for obese participants were not significantly higher than 50% chance level (one sample t-test, $t(18)=0.24$, $p=0.82$, 95% CI [-12%, 9%]). In contrast, in the healthy-weight group, performance between the high and low-calorie outcomes did not differ, $t(18)=0.58$, $p=0.57$, 95% CI [-16%, 9%], and mean accuracy was significantly higher than 50% chance level, $t(18)=3.3, p=0.004$, 95% CI [5%, 23%].
Figure 5: **Response -Priming Test.** Obese participants showed higher priming rates for high versus low-calorie outcomes. Performance did not differ for healthy-weight controls. White dotted line indicates 50% chance level. *\( p=0.006.\)

The RT analysis displayed no significant effects (all \( ps>0.18 \)).

**Refresher Instrumental Training.** During the final block of the refresher training the mean accuracy was 90% for the obese group (SD:17%) which did not differ significantly from the healthy-weight group mean accuracy 84% (SD:22%), \( t(36)=0.93, p=0.36, 95\% \text{ CI } [-19\%, 7\%].\)

**Outcome-Devaluation Test.** The ability of participants to select responses associated with still-valuable outcomes was examined during the outcome-devaluation test. The repeated measures ANOVA did not reveal any significant effects for the accuracy measurement (all \( ps>0.36 \)) nor for the RT (all \( ps>0.41 \)).
SOAT. One participant was excluded from the obese group as she did not understand the instructions and responded on all trials. For the remaining participants, ANOVA analyzed the mean percentages of responding to logos associated with devalued outcomes (no-go trials) and still-valuable outcomes (go trials) as a function of calorie content. This analysis revealed a main effect of value, $F(1, 35)=50.0$, $MSE=0.16$, $p <0.0001$, indicating that participants successfully responded more for stimuli predicting still-valuable outcomes (go trial mean response rate 72%, SD:28%) compared to devalued outcomes (no-go trials mean response rate 25%, SD:27%). There were no further significant effects (all $p$s>0.13), meaning that – contrary to our expectations - the two groups did not differ significantly in their ability to selectively withhold responses for devalued outcomes, nor was performance level related to the calorie content of the outcome. In a separate analysis, the same pattern of results was observed in the baseline test (main effect of value only, $F(1,35)=184$, $MSE=0.98$, $p<0.0001$).

Correlational Analyses. After confirming data distribution we correlated a number of variables with the mean high-calorie response-priming rates in separate group analyses. As can be seen in Table 2, no significant relationships were observed in either group between desire and the DBEQ external eating score, BIS total impulsivity score, or SSRT performance. However, we did find that higher impulsivity (SSRT) was related to poorer performance on both the SOAT and the baseline test.
Chapter 7

Table 2: Results from correlational analyses. See text for details.

<table>
<thead>
<tr>
<th>Variables in correlational analysis</th>
<th>Results</th>
</tr>
</thead>
</table>
| High-calorie priming x desire score | Obese group: $r(17)=-0.1, p=0.69$  
Control group: $r(17)=0.4, p=0.08$ |
| High-calorie priming x DBEQ EE | Obese group: $r(17)=-0.4, p=0.08$  
Control group: $r(17)=0.3, p=0.10$ |
| High-calorie priming x BIS total | $r(36)=0.1, p=0.72$ |
| High-calorie priming x SSRT | $r(36)=-0.1, p=0.41$ |
| Slips of action (difference score valuable – devalued) x SSRT | $\rho(35)=-0.4, p=0.01$ |
| Slips of action (baseline test; difference score valuable – devalued) x SSRT | $\rho(35)=-0.4, p=0.03$ |

Control Analyses. Three participants (from the control group) scored no better than 50% (chance level) during the final block of instrumental training. We repeated all of the above analyses after excluding these three participants. This did not change the observed pattern of results and, crucially, during the response-priming task we replicated the Calorie x Group interaction $F(1, 33)=4.2, MSE=0.07, p=0.05$.

As groups differed on reported stress and DBEQ external eating scores we repeated the response-priming test analysis entering these two factors as covariates. We replicated the Calorie x Group interaction $F(1, 34)=8.1,
$MSE=0.60$, $p=0.007$, with no significant effects involving the covariates (all $ps>0.23$).

Control-group participants were selected for analysis on the basis of demographic information (to rule out potential confounding effects of age and education level on response-priming rates). However, the analysis was repeated with inclusion of all 40 control-group participants who were of a healthy weight (BMI < 25 kg/m2). This did not change the observed pattern of results and during the response-priming task we replicated the Calorie x Group interaction $F(1, 57)=13.2$, $MSE=0.06$, $p=0.001$.

Finally, given that serotonin levels are known to affect performance on the slips-of-action task (Worbe, Savulich, de Wit, Fernandez-Egea, & Robbins, 2015) we replicated the analyses from the slips-of-action task after exclusion of the four obese participants who had a diagnosis of depression and were using SSRIs. The pattern of results was replicated, with only a significant main effect of value, $F(1, 31)=365.8$, $MSE=0.17$, $p<0.0001$.

4. Discussion
This study demonstrates that, for severely obese individuals, the biasing effects of external food cues on instrumental responding are particularly potent in the context of palatable, high-calorie food outcomes relative to low-calorie outcomes. When obese participants were shown pictures of potato chips or chocolate (or Pavlovian logos associated with these) they more frequently selected the key that had previously yielded the (signaled) food picture. By contrast, when presented with pictures of (or logos predictive of) lettuce and zucchini, obese participants pushed the two response keys equally often (scoring no better than chance level). Healthy-
weight controls did not show this differential pattern of responding for high- and low-calorie cues, and responded on the key associated with the presented/signaled picture regardless of calorie content. It has previously been suggested that these response-priming effects likely underlie maladaptive or addictive behavior (Colagiuri & Lovibond, 2014; Hogarth & Chase, 2011; Watson et al., 2014) and these results provide the first evidence that response priming by external stimuli is exaggerated in a clinical population, in the context of high- relative to low-calorie outcomes.

We found that logos previously associated with food pictures were able to trigger instrumental responses to the same degree as the food pictures themselves. The fact that food pictures and abstract stimuli predictive of these can bias choice (even after such limited training) reinforces the concerns that have been expressed about the obesogenic environment (Cohen, 2008; Harris et al., 2009; Swinburn et al., 2011). The finding that the motivating properties of food can generalize to stimuli that have been associated with that food, underscores the powerful influence of an environment that constantly signals the availability of unhealthy, calorie-dense food, and the challenge that it poses for those who struggle to resist this temptation.

Interestingly, in a previous study with the same paradigm, adolescents performed similarly to the obese group in the current study, demonstrating stronger response-priming effects in the context of high- relative to low-calorie outcomes (Watson et al., 2016). Given that the majority of the adolescents in that study were in the healthy BMI range, it raises interesting questions as to whether these associations can predict future behavior (and weight gain) or whether adolescents are hyper-sensitive to the rewarding
effects of tasty high-calorie foods as has been observed with financial rewards (Galvan, 2010; Van Leijenhorst et al., 2010). It remains to be seen whether the response-priming effects will change in this group as the motivational relevance of healthy food becomes more significant with age.

From a clinical perspective it is unclear how to weaken learned associations between cues, food and responses. Once established, these associations have been shown to bias choice towards the food that is being signaled to be available by one’s current environment *even when one is already fully sated on that food* (Watson et al., 2014). Furthermore, a recent MRI study provided evidence that this response priming effect is related to activity of the posterior putamen, a brain region that has previously been implicated in inflexible, habitual behavior (Bray et al., 2008). Finally, these associations appear to be highly persistent and resistant to extinction (reviews: Boutelle & Bouton, 2015; Bouton, 2011). However, given that bariatric surgery has been seen to reduce self-reported craving and striatal dopaminergic neural responses to palatable food pictures (Ochner et al., 2011, 2012; Scholtz et al., 2013), it remains possible that our group of obese individuals would post-operatively show a reduced response priming effect for high-calorie foods. As the motivational significance of healthier low-calorie foods increases, we would also expect response priming by low-calorie food outcomes to increase.

The current study used an associative learning framework to examine cue-elicited responding for food outcomes. The presence of high-reward outcomes during training is argued to strengthen the associations learned between outcomes and responses (and cues and outcomes), leading to stronger response priming at test for high-reward outcomes (Muhle-Karbe
& Krebs, 2012; Watson et al., 2016). Although we claim that this associative mechanism can provide insight into exactly how the obesogenic environment can bias behavior, this is by no means intended to be a full account of the processes leading to the development and maintenance of obesity, which is a highly complex condition. We expected some of the personality and behavioral measures, such as impulsivity, to offer further insight but this was not the case. We did not find any evidence of increased impulsivity in the obese group relative to the healthy controls, and obese individuals did not make any more slips of action in the presences of cues signaling devalued food outcomes. These unexpected results are in contrast to previous findings suggesting that obese individuals are less able to flexibly modulate responding on the basis of changes in outcome value (Coppin et al., 2014; Horstmann et al., 2015; Zhang et al., 2014) and are more impulsive (Mobbs et al., 2010; Nederkoorn, Braet, et al., 2006; Nederkoorn, Smulders, et al., 2006; Schag et al., 2013; Terracciano et al., 2009), particularly when examining impulsive responses directed towards food pictures (Houben, Nederkoorn, & Jansen, 2014; Nederkoorn, Coelho, Guerrieri, Houben, & Jansen, 2012). A possible explanation is that in the current study, only obese individuals without symptoms of BED were included and these did not, therefore, have a tendency towards compulsive behavior. The presence or absence of BED is not always assessed in studies of obesity although task performance can markedly differ (Schag et al., 2013; Voon et al., 2015) with one study providing evidence that obese individuals with BED relied on inflexible, ‘model-free’ decision-making whereas those without performed as well as healthy-weight controls (Voon et al., 2015). To conclude, the precise personality traits that characterize a clinical group of severely obese individuals and their vulnerability to food-associated cues remain to be illuminated.
In summary, this study is the first to provide evidence for the clinical relevance of this associative response-priming mechanism by demonstrating that it is exaggerated in obese individuals, particularly in the context of palatable, high-calorie food outcomes. Not only being confronted with food but even merely being reminded of it is enough to trigger instrumental behaviors directed towards that food. This means that our obesogenic environment with a plethora of cues signaling the availability of unhealthy foods can significantly impact behavior via learned associations, particularly in a vulnerable subset of individuals. Efforts should be made to prevent the formation of these associations and further investigate ways to disrupt them to reduce the impact of food cues on unhealthy food choices.