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ORIGINAL ARTICLE

Food-specific response inhibition, dietary restraint and snack intake in lean and overweight/obese adults: a moderated-mediation model

M Price¹, M Lee¹ and S Higgs²

BACKGROUND/OBJECTIVES: The relationship between response inhibition and obesity is currently unclear. This may be because of inconsistencies in methodology, design limitations and the use of narrow samples. In addition, dietary restraint has not been considered, yet restraint has been reported to moderate performance on behavioural tasks of response inhibition. The aim of this study was to investigate performance on both a food-based and a neutral stimuli go/no-go task, which addresses current design limitations, in lean and overweight/obese adults. The moderating role of dietary restraint in the relationship between body composition, response inhibition and snack intake was also measured.

SUBJECTS/METHODS: Lean and overweight/obese, males and females ($N = 116$) completed both a food-based and neutral category control go/no-go task, in a fully counterbalanced repeated-measures design. A bogus taste-test was then completed, followed by a self-report measure of dietary restraint.

RESULTS: PROCESS moderated-mediation analysis showed that overweight/obese, compared with lean, participants made more errors on the food-based (but not the neutral) go/no-go task, but only when they were low in dietary restraint. Performance on the food-based go/no-go task predicted snack intake across the sample. Increased intake in the overweight, low restrainers was fully mediated by increased errors on the food-based (but not the neutral) go/no-go task.

CONCLUSIONS: Distinguishing between high and low restrained eaters in the overweight/obese population is crucial in future obesity research incorporating food-based go/no-go tasks. Poor response inhibition to food cues predicts overeating across weight groups, suggesting weight loss interventions and obesity prevention programmes should target behavioural inhibition training in such individuals.

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INTRODUCTION

Growing evidence suggests that deficits in response inhibition tasks are related to calorie consumption¹ and obesity.² The go/no-go task and the stop-signal task (SST) are two commonly used measures of response inhibition. Typically, the go/no-go task involves presenting stimuli on a computer screen, with instructions to press a key when items from one category appear, but to withhold responses when items from another category appear. Response inhibition is indexed by the number of commission errors made (the number of times participants incorrectly respond to a 'no-go' trial). On the other hand, the SST requires participants to indicate from which of two categories a stimulus belongs, by pressing one of two response keys. On some trials, a stop signal is presented to indicate that no response should be made and response inhibition is measured using stop-signal reaction times.³

Although the go/no-go and SST tasks are often assumed to measure the same underlying construct, performance on these two tasks is weakly correlated,⁴ which suggests that they are assessing different aspects of response inhibition.⁵ In the SST, a motor response is activated on every trial with participants inhibiting an already initiated response. On the go/no-go task, there is no premotor initiation and participants decide each time if they need to respond.⁶ Therefore, the tasks differ in the gradation of inhibition that is required.⁷ In the SST, the motor response has

already been initiated before a contradictory instruction appears, which requires a later stage of inhibition. As go/no-go tasks reflect an early stage of inhibition, it is a viable target for intervention,⁸ and our focus here is on studies using the go/no-go paradigm, although it is important to note that similar inconsistencies exist in the SST literature (for a useful summary see Meule *et al.*⁹).

Many go/no-go tasks have used non-food-based stimuli (e.g., Guerrieri *et al.*,¹ Nederkoorn *et al.*² and Rosval *et al.*¹⁰). However, the dual-system approach to self-control suggests that both top-down inhibitory control and bottom-up food reward motivation interact to determine eating behaviour.^{11,12} Therefore, response inhibition tasks incorporating food-based stimuli are likely to be more informative.

In a go/no-go task with healthy food images as the 'go' category and unhealthy foods as the 'no-go' category, commission errors correlated positively with body mass index (BMI).¹³ However, this study lacked a control task including neutral stimuli and the sample was restricted to adolescent females. Consequently, Loeber *et al.*¹⁴ assessed commission errors on food-based and neutral no-go trials¹⁵ in male and female, lean and obese adults. They found that commission errors were greater when food stimuli were presented as a 'no-go' category than when the neutral stimuli were presented as 'no-go' category, but there were no differences between weight groups. However, the task used

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words rather than images, and the neutral words were not from one discreet category but from several categories. The authors proposed that the failure to find any differences between weight groups may have resulted from a category-size effect.¹⁶ Jasinska *et al.*¹⁷ conducted a large-scale study ($N=204$) of males and females using a food-based go/no-go task. Participants were presented with letters on the screen accompanied by either a healthy or unhealthy food image and told which were 'go' and which were 'no-go' cues. Although there were associations with eating behaviour, no relationship between BMI and commission errors was reported. Meule *et al.*¹⁸ used a go/no-go task with letters as targets, accompanied by distractor images, and examined the effects of unhealthy food versus neutral images. Commission errors did not differ between stimulus types (food versus neutral), contrary to Loeber *et al.*¹⁴ However, this study only tested young, lean females, which restricts generalisability. Further, the task may have confounded attentional processes with response inhibition processes¹⁸ and using a paradigm where food images are the target stimuli may be more appropriate.¹⁹ Meule *et al.*⁹ designed a go/no-go task with food and non-food images and found that BMI was positively correlated with commission error difference scores (the difference between number of errors on the food versus neutral no-go trials), but the young, female, lean sample again makes generalisation difficult. In addition, the neutral images were from various categories and so the possibility of category-size effects cannot be ruled out.

Given the methodological limitations of previous research, it is unsurprising that a clear relationship between food-specific response inhibition and overweight has not yet emerged. This may be because of possible moderators that may influence the link between response inhibition and BMI, for example, dietary restraint. Dietary restraint is the effortful restriction of caloric intake to lose weight or prevent weight gain. Attempts to restrain are often successful only in the short term and restraint has been linked to overconsumption after food cue exposure^{20,21} and higher BMI.^{22,23} Restrained eaters show altered neural responses to food cues in event related potential components related to response inhibition in a food-based go/no-go paradigm^{24,25} and when low in response inhibition, restrained eaters have been shown to eat more in the laboratory.²⁶ However, Meule *et al.*⁶ reported that high dietary restrainers made fewer commission errors, but consumed more snacks in a 'taste-test' after a preload. This suggests that participants high in dietary restraint may be well practiced in short-term avoidance of food and perform well on food no-go tasks but that restraint may give way to disinhibited eating once exposed to food via a preload.²⁷ Conversely, Houben and Jansen⁸ did not provide a preload and found that restrained eaters who completed a chocolate no-go task, subsequently ate less chocolate than unrestrained eaters, suggesting that cues to inhibit eating (such as a chocolate 'no-go' task) reduce consumption in restrained eaters. Although it is often assumed that poor response inhibition is related to greater intake of palatable food, this has only been shown experimentally in lean populations and dietary restraint has not been taken into consideration as a moderator.

Taken together, research to date suggests that response inhibition deficits may be associated with overeating and obesity, but the picture is not clear; this may be because of both methodological limitations and variations in dietary restraint. We addressed the methodological limitations of previous research by including: (1) a go/no-go task with food images as the target stimuli rather than a distractor so as to avoid confounding response inhibition with attentional processes; (2) a single-category, neutral control task for comparison; (3) a sample of males and females with wide ranging adiposity and age so that findings are more generalisable and can be compared across weight groups; (4) a disguised taste-test to assess the relationship

between response inhibition and actual intake; and (5) a measure of dietary restraint to assess its role in moderating task performance.

We predicted that commission errors would be greater in the overweight/obese participants, and that poorer response inhibition would predict greater snack intake. However, we also predicted that dietary restraint would moderate this relationship, such that overweight, restrained eaters would make fewer commission errors and consume fewer snacks than unrestrained eaters. We tested whether this model held for both the food-based and the neutral go/no-go task.

SUBJECTS AND METHODS

Participants

Data were collected from 116 participants (females=94) recruited from the student population at the Swansea University and the local community (mean age = 26.0 (10.65); 18–69 years; mean BMI = 24.2 (4.31); 17.6–41.4 kg m⁻²). Poster and email advertisements asked for volunteers for a study on 'Mood, Cognition and Taste Perception'. Participants could not take part if they had any medical conditions affecting appetite or if they were intolerant or allergic to any foods. One participant declined to have their body composition measured, and so for the subsequent analysis $N=115$. The study was approved by the Department of Psychology Research Ethics Committee at Swansea University. Participants were reimbursed with course credit or £6 payment.

Measures

Go/no-go task. Both the neutral and food-based go/no-go tasks were programmed using the E-Prime 2.0 software (Psychology Software tools, Inc., Sharpsburg, PA, USA; see Figure 1). Participants were instructed to press the space bar in response to explicitly instructed 'go' stimuli and withhold any response to 'no-go' stimuli. In the neutral task, sports equipment images were presented as the 'no-go' stimuli and toiletries as

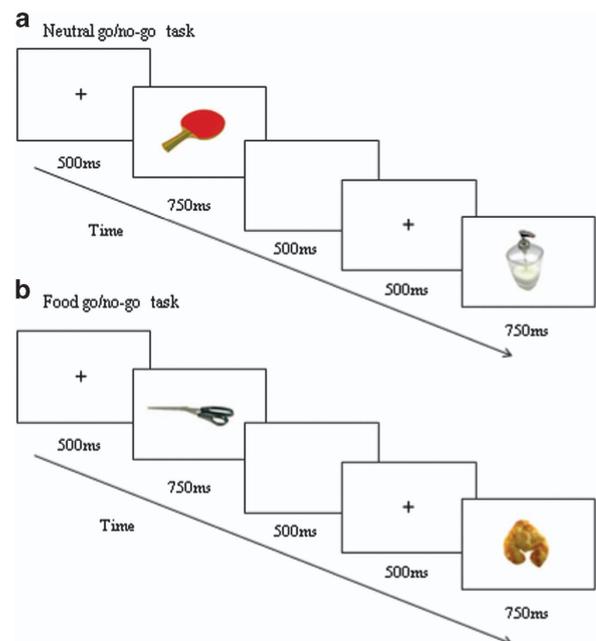


Figure 1. Go/no-go task: A total of 200 trials were presented, 100 (in two blocks of 50) for the neutral task (a) and the same for the food task (b). Images were presented using a ratio of 80% 'go' to 20% 'no-go' trials to create a prepotent 'go' response. Each trial was presented for 750 ms and was separated by a blank screen for 500 ms and preceded by a fixation point for 500 ms. The go and no-go categories were presented in a pseudorandomised order, with 3, 4 or 5 go trials in between every no-go trial. Presentation order of the food and neutral tasks was fully counterbalanced.

the 'go' stimuli. In the food-based task, high-energy dense food images were presented as 'no-go' targets, and neutral office supplies as 'go' targets. The stimuli were selected from the BOSS database of normative photographs of objects.²⁸ The BOSS images are normalised for category, familiarity, visual complexity, object agreement and viewpoint agreement, making them equivalent in valence and perceptual characteristics.²⁸ The 'go' category in the neutral task differed to that used in the food task to reduce the likelihood practice effects. All participants completed both tasks and the presentation order was fully counterbalanced. The measure of interest was the number of commission errors (responses incorrectly made to 'no-go' trials).

Disguised taste-test. Participants were asked to sample three types of biscuit and rate them for pleasantness, strength of flavour and crunchiness on separate visual analogue scales. They were informed that they may eat as much as they liked because any food left over would be discarded. The biscuits were McVities milk chocolate digestives (2071 kJ (495 kcal)/100 g); Maryland chocolate chip cookies (2040 kJ (487 kcal)/100 g); McVities Hobnobs (1968 kJ (470 kcal)/100 g). The biscuits were broken up into small pieces and presented in three separate bowls. To minimise social desirability effects, the researcher left the room for 5 min, while the participant completed the test. The biscuits were weighed before and after to measure total consumption (in g; to 2 decimal places) using Sartorius 3102S scales.

Dietary restraint. The dietary restraint subscale of the Dutch Eating Behaviour Questionnaire (DEBQ; van Strien *et al.*²⁹) assesses the extent to which a person restricts their food intake to maintain/lose weight. It has 10 items, for example, 'When you have put on weight, do you eat less than you usually do?' The Cronbach's α for the current sample was 0.91.

Adiposity. BMI is commonly used as a measure of overweight and obesity, but a limitation is that it does not take muscle mass into account. Here we use body composition instead of BMI to define overweight and obesity using a TANITA BF-350 body composition analyser (Tanita Europe, Amsterdam, The Netherlands), which is based on bioelectrical impedance analysis. Participants were selected for inclusion in either the 'lean' ($N=83$; males = 16, females = 67) or 'overweight/obese' ($N=32$; males = 6, females = 26) weight group, based on standard body composition health guidelines, adjusted for age and gender, for percentage body fat considered to be 'underfat/healthy' or 'overfat/obese', respectively (NIH/WHO guidelines reported in Gallagher *et al.*,³⁰ NY Obesity Research Centre).

Procedure

All participants were instructed to eat their normal meal between 2 and 3 h before the study. This was to make sure that extreme states of hunger were avoided as this has been shown to affect food go/no-go task performance.³¹ After obtaining consent, each participant filled out a brief mood questionnaire to maintain the cover story. This was based on 10 items selected from the POMS-SF (Profile of Mood Sates—Short Form; Curran *et al.*³²). Participants were asked to indicate on a scale of 1–5 to what extent each of the 10 adjectives (e.g. lively, confused, tense, etc.) described their current mood, ranging from 'Not at all' to 'Extremely'. Participants then completed a paper-based visual analogue scale to assess current hunger. They were asked to place a mark along a 100 mm line from 'not at all hungry' to 'extremely hungry' in response to the question: 'How hungry do you feel right now?' After completing both go/no-go tasks, the participants moved to an adjacent area to complete the taste-test. They then completed the DEBQ dietary restraint subscale and basic demographic information. As alcohol consumption has been related to response inhibition in previous studies,³³ this was also recorded along with height, weight and a measure of percentage body fat. All participants were fully debriefed and paid £6 or administered course credit.

Analysis plan

Examination of data distribution using z-score analysis and boxplots revealed that for commission errors on the food task, there were four outliers, and on the neutral task, there were two outliers, all with scores >2.5 s.d. above the mean. It was likely that these participants were not paying attention to the tasks and their removal resulted in a normal distribution for parametric analysis (z -skewness <2.5).

PROCESS³⁴ software was used to test the predicted model (see Figure 2). The moderated-mediation analysis for the commission errors made on the

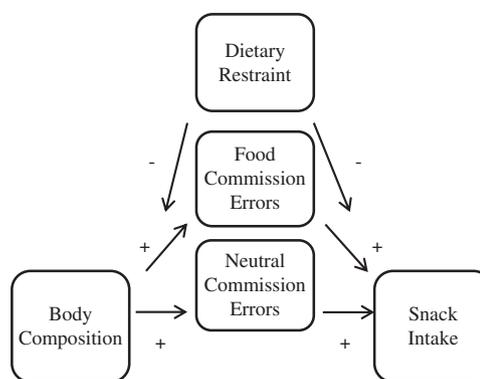


Figure 2. Proposed moderated-mediation model for the food-based and neutral go/no-go tasks. An indirect pathway between body composition (lean versus overweight/obese), commission errors made on the food-based go/no-go task and the neutral control go/no-go task, and snack intake. The model is tested at three levels of DEBQ dietary restraint (mean \pm 1 s.d.). The +/– symbol denotes the expected direction (positive or negative) of the relationship.

food-based and neutral stimuli tasks were run in parallel using PROCESS Model 58 with 5000 bootstrap samples. All variables showed low (<1.1) variance inflation factor and so the model met the criteria for multicollinearity. Continuous variables were also mean centred as recommended by Howell.³⁵ All analysis was conducted using the SPSS 20.0 software (IBM Corp., Armonk, NY, USA).

RESULTS

As previous research suggests that alcohol consumption and hunger are related to response inhibition^{31,33} and because both variables correlated significantly with commission errors made on the food task ($r = -0.203$; $P = 0.02$; $r = -0.16$; $P = 0.04$ respectively) in the current sample, we included both variables as covariates in the model. In addition, as dietary restraint is often higher in women,³⁶ gender was also controlled for in the model.

Task comparison

Related t -test showed that participants made significantly more commission errors on the neutral no-go trials than on the food no-go trials ($t(115) = 5.31$; $P < 0.0001$). $N = 13$ made no errors at all on the food-based task and $N = 7$ made no mistakes at all on the neutral task.

Moderated-mediation analysis

Body composition was entered as the predictor variable (coded lean = 1; overweight/obese = 2), commission errors on the food-based task or the neutral control task were entered as the mediating variables acting in parallel, snack consumption (g) was entered as the dependent variable and dietary restraint scores as a moderating variable. The model output gives us information not only on the indirect pathway between body composition and overeating but also on the direct pathways between body composition and commission errors, and the direct pathway between commission errors and intake. It also gives us information about the moderating role of restraint. Therefore, within one model we obtained three sets of analysis: (1) the relationship between overweight and commission errors and the moderating role of restraint; (2) the relationship between commission errors and intake and the moderating role of restraint; and (3) mediation: the indirect route between overweight and intake through commission errors, and the moderating role of restraint. These are now reported in turn.

For the pathway between body composition and commission errors on the food-based task, the interaction between body

composition and restraint was significant ($b = -1.0$, $s.e. = .42$, $t = -2.4$, $P = 0.02$, 95% confidence interval (CI) = -1.83 to -0.17). To probe the nature of the interaction, high and low levels (± 1 s.d.) of dietary restraint were plotted for lean and overweight/obese groups (see Figure 3a). Overweight/obese participants made significantly more errors than the lean participants, but only when they were also low (-1 s.d.) in restraint ($b = 1.26$; $t = 2.44$, $P = 0.02$, $CI = 0.24$ – 2.2) and not when they were high ($+1$ s.d.) in restraint ($b = -0.15$; $t = -0.36$, $P = 0.72$, $CI = -0.99$ to 0.69). Restraint did not moderate the number of commission errors made in the lean group ($b = -0.17$; $t = -0.94$, $P = 0.35$, $CI = -0.52$ to 0.18). There was no significant main effect of body composition or restraint in predicting commission errors in the neutral task and no interaction ($P > 0.05$; see Figure 3b).

For the pathway between commission errors on the food-based task and intake, there was a significant main effect of commission errors ($b = 1.75$, $t = 2.23$, $P = 0.03$, $CI = 0.19$ – 3.31), but the main effect of restraint ($b = 0.55$, $t = 0.49$, $P = 0.63$, $CI = -1.69$ to 2.79) and the interaction between commission errors and restraint ($b = -0.95$, $t = -1.15$, $P = 0.25$, $CI = -2.59$ to 0.68) were not significant. There was no significant main effect of commission errors made on the neutral task or restraint for predicting intake and no interaction ($P > 0.05$).

Table 1 shows the bootstrap confidence intervals for an indirect pathway between body composition and intake, through commission errors, at three levels of restraint (mean ± 1 s.d.) for both the food-based and neutral go/no-go tasks. A significant pathway is represented by bias corrected CIs that do not pass through zero. This was only the case for low levels of restraint in the food-based task. Therefore, the indirect pathway between body composition and snack intake, through food commission errors, was significant only at low levels of restraint. The direct pathway between body

composition and intake was not significant ($b = 2.16$, $t = 1.02$, $P = 0.31$, $CI = 2.02$ – 6.3). Figure 4 illustrates the significant pathways.

Removing the covariables resulted in the mediation falling below the 95% CI and so they were retained in the model.

DISCUSSION

This study investigated the relationships between body composition, response inhibition and snack intake in one model. We found that (1) overweight/obese participants showed poorer response inhibition on a food-based go/no-go task than lean participants;

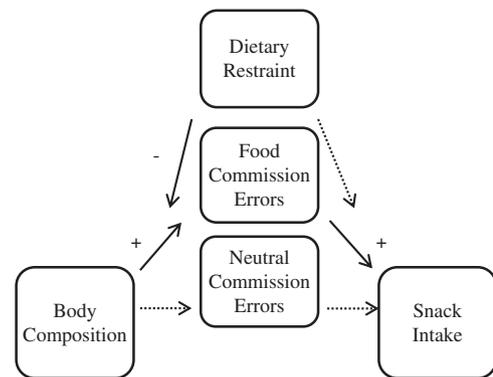


Figure 4. Significant pathways in the moderated-mediation model for the food-based and neutral go/no-go tasks (controlling for baseline hunger, gender and alcohol consumption). Significant pathways are denoted by solid arrows ($P < 0.05$), and nonsignificant pathways are denoted by dotted arrows. The +/- symbol denotes the direction (positive or negative) of the relationship.

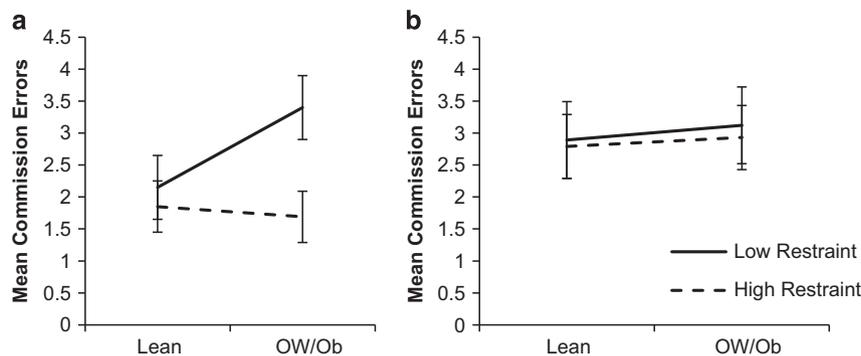


Figure 3. Mean (and s.e.) commission errors made on the food-based (a) and neutral (b) no-go trials by participants in the lean versus overweight/obese (OW/Ob) groups, at high and low (± 1 s.d.) levels of dietary restraint (DEBQ).

Commission errors	Restraint level (DEBQ)	Effect	S.e.	Lower-level confidence intervals	Upper-level confidence intervals
Food no-go trials	Low	3.69	2.30	0.40	10.05
	Medium	0.97	0.86	-0.09	3.52
	High	-0.29	0.89	-3.41	0.55
Neutral no-go trials	Low	-0.87	1.36	-5.94	0.47
	Medium	-0.29	0.48	-2.23	0.17
	High	-0.01	0.58	-1.54	0.91

Abbreviation: DEBQ, Dutch Eating Behaviour Questionnaire. Bias corrected bootstrap 95% confidence intervals for an indirect pathway between percentage body fat and snack intake, through commission errors made on either the food-based or neutral control go/no-go trials, at three levels of restraint (mean ± 1 s.d.). The significant indirect pathway is in bold.

however, this was only the case for those participants low in dietary restraint; (2) poorer response inhibition predicted higher biscuit intake across weight groups and restraint status; and (3) overeating in overweight/obese participants, low in restraint is fully mediated by poorer response inhibition to food. Response inhibition to neutral stimuli was not related to adiposity or snack intake and there was no moderation by dietary restraint.

The present results are consistent with previous reports that response inhibition deficits on a food go/no-go task correlate with BMI in a sample of adolescent females.¹³ However, we extend this finding to a wider sample and shed further light on the nature of the relationship by showing that it is specific for food cues and moderated by dietary restraint. Loeber *et al.*¹⁴ found no differences between weight groups for response inhibition to food-based or neutral no-go trials, which is contrary to the current findings. This may be because they used words instead of images and did not assess dietary restraint.

Meule *et al.*⁶ found that dietary restraint improves performance on both food-based and neutral no-go trials in lean participants, but we extend these findings to overweight and obese participants. However, our finding that restraint does not moderate performance in the lean participants or on a neutral stimuli task in either lean or overweight participants is contrary to Meule *et al.*⁶ findings. This may be because of task and sample differences between the two studies. For example, Meule *et al.*⁶ used a multiple category control and the images were distractors and not targets, whereas we used a single-category neutral control, and used images as targets not distractors. The current task design is therefore sensitive to response inhibition differences between weight groups and levels of restraint and would be more useful in future obesity-related research.

In the current study, we found that reduced response inhibition in the food (but not the neutral) no-go trials predicted greater snack intake. Although much of the literature assumes that there is a relationship between response inhibition and intake and studies that have used the go/no-go and SSTs to train response inhibition have been shown to reduce intake,^{8,37,38} a link between baseline response inhibition and snack intake in a sample including overweight/obese individuals has not previously been established. Most studies have focused on the relationship between obesity and response inhibition^{2,13,14,39} or used a lean sample to investigate differences between food and neutral cues.^{9,40} One study that measured intake⁶ found that low restrainers consumed less than high restrainers; however, in the present study, we did not find this to be the case. This may be the result of the use of different scales to measure restraint. In the current study, we used the restraint subscale of the DEBQ,²⁹ whereas Meule *et al.*^{6,9,18} used the Restraint Scale (RS; Herman *et al.*⁴¹). When levels of restraint have been measured using the RS, it has been reported that high but not low restrainers tend to over eat following a preload of food or a negative mood induction.^{20,21} The DEBQ differs from the RS as it excludes references to weight fluctuation and overeating and describes specific strategies for reducing caloric intake.⁴² Westenhoefer⁴³ introduced the idea of flexible versus rigid restraint: flexible restraint is related to more successful weight loss and rigid restraint (an 'all or nothing' approach to dietary restraint) results in greater attentional bias towards food and less weight loss.⁴⁴ Although restraint as measured by both scales appears to relate to enhanced response inhibition to food cues, restraint on the DEBQ in the current study was not related to consumption, whereas high restraint on the RS resulted in increased consumption in the study of Meule *et al.*⁶ Therefore, the role of dietary restraint in moderating the relationship between response inhibition and overeating may be dependent on the definition and measurement scale used.

We used a single-category neutral no-go control (sports equipment) and found that participants made fewer errors on

the food no-go trials compared with the neutral no-go trials. This is consistent with previous studies.^{9,14,45} For example, Mobbs *et al.*³⁹ reported more errors in response to neutral versus food words in a sample of obese adults and normal weight controls and suggests that regardless of weight group, there is a tendency to make fewer errors when food is the no-go target than when the no-go target is neutral. This may be because food images, having high motivational value, are preferentially processed relative to neutral cues.⁴⁶ Our results suggest that it is individual differences in the ability to inhibit responses to these highly salient food cues that is related to overeating and overweight and not response inhibition in general.

Response inhibition is also commonly measured using the SST and previous studies have investigated food-based versus general task performance^{40,47} in relation to overweight,^{2,3,48} intake^{38,40,49} and dietary restraint.^{40,49,50} However, no study has combined these variables into one model using the SST and this may be a useful direction for future research. The SST and go/no-go tasks are only weakly correlated and are likely to be tapping into different stages of response inhibition and whether this model would hold for SST outcomes is currently unknown.

A limitation of the study was that the overweight/obese and male participants were under-represented. However, we still retained an adequate sample size for the overweight/obese group with power to detect differences between weight groups. Although the male sample was small, there was equal distribution across weight groups, and gender was controlled for in analysis; however, future research would benefit from studying the relationship between response inhibition, overweight and intake in larger male samples as this group has been under studied in the literature.

It would also be useful to assess the relative effectiveness of response inhibition training in high and low restrainers in the overweight/obese population. Houben and Jansen⁸ found that high restrainers ate less chocolate after chocolate no-go, response inhibition training, but this was in lean participants. If overweight restrainers already perform well in the short term; perhaps, we would see an effect of training only in those participants low in dietary restraint. However, it has been noted that restraint is an exhaustive resource and likely to result in relapse.⁵¹ Thus, while the restrained overweight and obese participants in the present study had better response inhibition to food cues than the low restrainers, this level of cognitive control may not be sustainable in the long run. Other techniques that do not rely on effortful inhibition may be more effective for helping with control of impulsive behaviour around food. An emerging research area for promoting self-control is the use of implicit priming techniques. For example, priming higher level construal thinking has been shown to enhance self-control⁵² and reduce snack intake,⁵³ and does not require demanding inhibitory resources. This may be useful for both short-term improvement in low restrainers and longer-term success for high restrainers in real-world settings. In summary, for the first time in a single model, we show that being overweight and low in dietary restraint is related to poorer response inhibition to food (but not neutral) cues. We also demonstrate that poorer response inhibition to food (but not neutral) cues predicts increased snack intake, suggesting that overweight/obese groups, low in restraint, may benefit most from response inhibition training interventions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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