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Enhancing inhibitory learning to reduce overeating: Design and rationale of a cue exposure therapy trial in overweight and obese women

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ABSTRACT

The prevalence of overweight and obesity has increased substantially over the last decades. Weight loss attempts in overweight individuals are common, though they seldom result in successful long-term weight loss. One very promising treatment is food cue exposure therapy, during which overweight individuals are repeatedly exposed to food-associated cues (e.g., the sight, smell and taste of high-calorie foods, overeating environments) without eating in order to extinguish cue-elicited appetitive responses to food cues. However, only few studies have tested the effectiveness of cue exposure, especially with regards to weight loss. For exposure treatment of anxiety disorders, it has been proposed that inhibitory learning is critical for exposure to be effective. In this RCT, we translated techniques proposed by Craske et al. (2014) to the appetitive domain and developed a novel cue exposure therapy for overeating aimed at maximizing inhibitory learning. The current RCT tested the effectiveness of this 8-session cue exposure intervention relative to a control intervention in 45 overweight adult (aged 18–60) females at post-treatment and 3-month follow-up, of which 39 participants completed the study. Weight loss, eating psychopathology, food cue reactivity, and snacking behaviour were studied as main treatment outcomes, and mediators and moderators of treatment effects were studied. The presented study design represents an innovative effort to provide valuable clinical recommendations for the treatment of overeating and obesity.

1. Introduction

A large proportion of overweight and obese individuals engage in weight loss attempts [1]. However, successful long-term weight loss seems very difficult to achieve: it has been estimated that only 20% of overweight individuals are successful at losing at least 10% of their initial weight and maintaining this loss for at least one year [2]. A major cause of eating more than physiologically needed is thought to be an increased reactivity to food cues. This food cue reactivity includes anticipatory psychological (i.e., craving) and physiological (e.g., increased salivation) responses that prepare an organism for food intake and promote (over)eating [3]. Overweight individuals and binge eaters show greater reactivity to food cues (e.g., [4,5]), while reactivity seems to be reduced in successful weight loss maintainers [6]. This suggests that aiming to diminish food cue reactivity during treatment might effectively reduce overeating and promote weight loss.

Food cue reactivity is at least partly learned (e.g., [7]): food cues (conditioned stimuli or CSs; e.g., the smell and sight of food) have become associated with eating (unconditioned stimulus or US) through repeated pairings, and these CSs can subsequently elicit cue reactivity. Similarly, learning models predict that extinction of cue reactivity can be achieved through repeated exposure to CSs without the US (eating), thereby lowering cue-elicited motivation to eat (e.g., [8,9]). This is the aim of cue exposure therapy, in which individuals with overweight and/or eating disorders are repeatedly exposed to their personal food cues without eating. Studies on cue exposure therapy are scarce, though the limited findings indeed show substantial reductions in cue-elicited cravings and eating binges (e.g., [10-15]). However, whether cue exposure is also effective in facilitating weight loss remains unclear. Moreover, although a long-term abstinence of binge eating has been found [11,15], returns of cravings and overeating at follow-up have also been reported [10], suggesting that cue exposure therapy might require optimization in order to have long-lasting effects.

The finding that appetitive responses can return after treatment is line with the idea that during extinction, the original CS-US association is not destroyed. Rather, a new association is formed: CS means no US [16,17]. This inhibitory CS-noUS association is relatively fragile and context-dependent, which is why responses can return even when they have been successfully extinguished. Hence, strengthening inhibitory CS-noUS associations in cue exposure therapy may help improve long-term outcome. For the treatment of anxiety disorders, Craske and colleagues [18] have recently proposed a number of exposure techniques to achieve this. One example is to design exposure sessions in a way that maximizes the violation of CS-US expectancies – if the non-occurrence of the US is surprising, this should strengthen (inhibitory)

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learning. In cue exposure, this may be achieved by identifying a patient's specific overeating cues that are linked to strong eating expectancies [e.g., "If I am home alone and I feel sad (CS), I will have an eating binge (US)"] and exposing the patient to these exact cues while facilitating attention to both the cues and the non-occurrence of the US (eating). This expectancy violation approach contrasts with the classical habituation approach, in which exposure sessions are targeted on lowering anxiety (or eating desires). Habituation during exposure sessions has been shown to be non-predictive of treatment outcome [14,19], though it remains an empirical question whether expectancy violation *is* important for treatment outcome in cue exposure therapy. Another interesting technique proposed by Craske and colleagues is occasional reinforced extinction: occasionally reinforcing the CS-US contingency might allow reinforced trials to be associated with extinction, leading to attenuated returns of responses. In cue exposure therapy, occasionally eating small amounts of food may reduce overeating by associating eating a small amount of food with no further intake (see [20,21]).

1.1. Objectives

The main aim of this RCT was to investigate the effects of a cue exposure intervention that is based on the inhibitory learning-based techniques proposed by Craske et al. [18] and aimed at achieving long-term reductions in overeating and weight in overweight individuals. An active control intervention was included aimed at improving lifestyle. As primary objective, it was studied whether participants who received the cue exposure vs. control intervention would lose more weight, show larger reductions in eating psychopathology and food cue reactivity, and consumed less high-calorie snack foods, both at post-treatment and at follow-up. As a secondary objective, it was studied whether the cue exposure vs. control intervention would show increased response inhibition and self-control, and less attentional bias towards high-calorie foods. Further, it was studied whether the effects on treatment outcome were mediated by expectancy violation, while habituation was not expected to play a role in treatment outcome. Finally, response inhibition and self-control, good sleep, and attentional bias were expected to be treatment outcome moderators.

2. Material and methods

2.1. Overview of study design

Participants were screened for eligibility and randomized to either an 8-session cue exposure intervention or an active control intervention (Lifestyle+). Measurements were conducted at pre-measurement, during the intervention, at post-measurement, and at three months follow-up (Fig. 1). The study was approved by the Ethical Committee of the Faculty of Psychology and Neuroscience of Maastricht University (148_07_10_2013_A3).

2.2. Participants and inclusion/exclusion criteria

Participants were overweight and obese individuals. The inclusion criteria included: a female gender, a Body Mass Index (BMI) of at least 27, and an age between 18 and 60 years. A BMI cut-off of 27 was used to avoid including participants who were borderline overweight. Females were included to facilitate comparability with a previous study [14], and to reduce variability in responses. Participants were also required to be highly motivated to lose weight: motivation to lose weight was verbally indicated on a 10-point scale, and participants had to indicate a minimum motivation of "8" to be eligible for participation. In addition, participants had to indicate experiencing a clear difficulty to refrain from eating palatable high-calorie snack foods. The exclusion criteria were: suffering from self-reported smelling problems (indication of anosmia) since smelling is an important part of the cue exposure intervention, pregnancy, currently receiving psychotherapeutic or psychopharmacological treatment, bariatric surgery (pre and post-operative), and insufficient time for the intervention and measurements. As shown in Fig. 1, of 75 interested participants that were informed about the study, 49 participants were eligible based on the abovementioned criteria.

2.3. Recruitment and retention

Participants were recruited in and around Maastricht through advertisements in local newspapers and gyms, and through flyers. Interested participants were carefully screened for eligibility during a phone interview. Participants received € 25, - for every completed measurement (pre, post, and follow-up). At follow-up, participants received another € 25, - as an additional incentive if they had attended all therapy sessions and measurements. In order to minimize drop-out after the post-measurements, participants were contacted by phone one month before the follow-up measurements to plan the last sessions, and to underline the importance of completing the study. The study was conducted from January 2015–December 2015.

2.4. Procedure

For each measurement (pre, post, and follow-up), participants attended the university on two separate sessions. It was attempted to minimize the time between both sessions, with a maximum of two weeks.

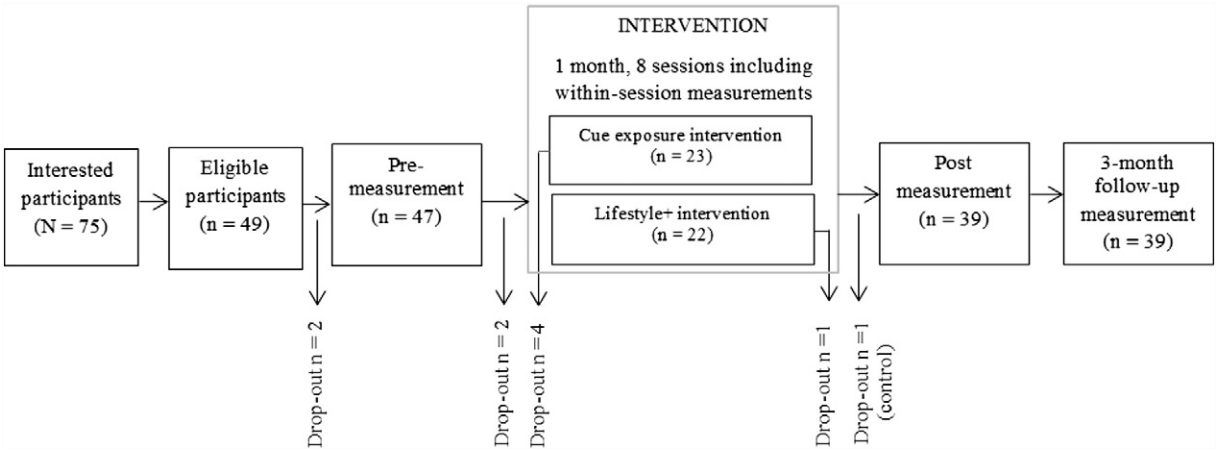

Fig. 1. Overview of the study design and sample size.

2.4.1. Session 1

To standardize hunger, participants were asked to consume a small meal (e.g., one sandwich) 1 h prior to the start of the session. After arrival, participants received information regarding the set-up of the study and gave written consent. Next, a baseline hunger VAS was completed, followed by baseline food cue reactivity measures (desire to eat VAS, salivation, and prospective portion size). After this, the food cue reactivity task was administered. Participants were exposed to the sight and smell of one of ten snack foods: Lay's salty crisps, Lay's paprika-flavoured crisps, M&Ms. with or without peanuts, Cote d'Or milk chocolate with or without hazelnuts, Cote d'Or dark chocolate, Katja liquorice, Duyvis spiced nuts, and Red Band wine gums. These ten foods were based on the ten most frequently mentioned favourite food items in a female overweight sample from a previous study [14]. Participants were instructed to select their favourite food from this list of foods (FF-list). The exposure task lasted exactly 3 min, and the experimenter modelled the exposure. At minute one, participants completed a desire to eat VAS. At minute two, salivation was measured. At minute three, prospective portion size was assessed. After the food cue reactivity task, the Stop-Signal Task was administered, followed by a hunger VAS. Next, only at pre-measurement, participants completed an appetitive conditioning task. At the post and follow-up measurements, participants now completed the bogus taste test. Finally, participants completed another hunger VAS, and the EDE-Q (pre-measurement and follow-up only).

2.4.2. Session 2

To standardize hunger, participants were asked to consume a small meal 2 h prior to this session. Upon arrival, participants completed a hunger VAS. Next, participants completed the attention bias task, wrote down when they last ate, and then completed the Self-Control Scale. After this, the binge eating interview was conducted. Only at pre-measurement, this interview was followed by the CS-US interview. The CS-US interview was developed specifically for this study in order to compose the personalized CS-US expectancy items and to identify relevant USs (regular unwanted consumption of unhealthy high-calorie snacks or binge foods) and CSs (e.g., environment, time of the day, feelings, thoughts) for the exposure intervention. The two most favourite snack foods were identified during the interview, of which one would be included (FF-personal exposed) and one would not be included in the exposure exercises (FF-personal non-exposed). After the interview(s), the participant's weight and height was measured.

2.4.3. Therapy sessions

At the start of each therapy session (cue exposure and Lifestyle +), a baseline hunger VAS and a desire to eat VAS were administered. In addition, desire to eat VASs was administered every minute during exposure exercises.

2.5. Measurements

Primary outcome measures were weight loss, eating psychopathology, food cue reactivity, and snacking behaviour during a bogus taste test. Secondary outcome measures were response inhibition, self-control, and attentional bias. Expectancy violation was investigated as a mediator between condition and treatment outcome. Habituation of food cue reactivity, attentional bias, response inhibition and self-control, and sleep quality were investigated as moderators for treatment success [19,22-25], and interrelations between attentional bias and inhibitory and self-control measures were studied [26]. An appetitive conditioning task was administered only at pre-measurement for comparison with a normal-weight sample. For an overview of all measurements and the time point of administration, see Table 1. The measurements were conducted by PhD students and psychology students who were obtaining their master degree. They were blinded to the assigned intervention group.

2.5.1. Primary outcome measures

2.5.1.1. Weight loss. Weight loss at post and follow-up measurement was calculated by the change in percentage of weight relative to pre-measurement: a larger negative score reflecting more weight loss.

2.5.1.2. Eating psychopathology. The Eating Disorder Examination Questionnaire (EDE-Q; [27]) is a widely-used self-report questionnaire that assesses disordered eating behaviours and attitudes over the previous 28 days. It consists of 28 questions which are each scored on a 7-point scale, with higher scores reflecting greater levels of eating psychopathology. Binge eating was further assessed during a semi-structured interview that was created for this study (binge eating interview), using the DSM-V criteria [28].

2.5.1.3. Food cue reactivity. Food cue reactivity was assessed by measuring desire to eat, salivation and prospective portion size before and after exposure to FF-list. Desire to eat was measured on a VAS ("*How strongly do you desire palatable food right now?*"), ranging from 0 (*no desire at all*) to 100 (*very strong desire*). Salivation was measured using cotton rolls (Hartmann, nr 2, 10 × 35 mm). Participants placed the cotton roles between the cheek and lower gum on the left and right side for exactly 1 min. The dental rolls were kept in a sealed plastic bag, which was weighed before and after saliva collection using a weighing scale accurate to 0.01 g (Mettler Toledo, PB3002). The prospective portion size task served as a behavioural measure of food cue reactivity. In this task, an empty bowl was presented on a computer screen, and participants selected their desired prospective portion size of FF-list. Participants could adjust the amount of FF-list in the bowl: by moving a marker on a horizontal line to the right, the bowl filled, and by moving the marker to the left, the bowl emptied. Participants were instructed to select as much of FF-list as they would like to eat at that moment in

Table 1
An overview of all measurements and the time points of administration during the study.

Measures	Pre-measurement	During the intervention	Post-measurement	Follow-up measurement
Weight	X		X	X
Binge eating	X		X	X
Eating Disorder Examination Questionnaire [27]	X			X
Expectancy violation (CS-US expectancies)	X		X	X
Food cue reactivity	X		X	X
Snacking behaviour (bogus taste test)			X	X
Stop-Signal Task [29]	X		X	X
Baumeister Self Control Scale [30]	X		X	X
Attentional bias [31]	X		X	X
Within and between-session habituation		X		
Pittsburgh Sleep Quality Index [32]	X		X	X
Appetitive conditioning	X			

time. The amount selected was converted to kcal and served as dependent variable.

2.5.1.4. Snacking behaviour. To assess snacking behaviour, participants completed a 10-min bogus taste test. The taste test was personalized for each participant, and consisted of three personal favourite snack foods. Two of the test food items were incorporated during cue exposure therapy (FF-list and FF-personal exposed). In addition, a third personal favourite food item was used in the taste test which was not incorporated during cue exposure (FF-personal non-exposed). The non-exposed food item was included to test whether the effects of cue exposure on food intake would generalize to other, non-exposed, foods. As a cover story, participants were presented with two supposedly slightly different versions of the three types of foods (six bowls of food in total), and were asked to taste these foods and answer questions about the differences between the two versions of each food (e.g., "*Which is stronger in flavour?*"). In reality, the two 'versions' were identical. Participants were instructed that they can taste as much of the foods as they like, and that they have to remain seated until the experimenter returns.

2.5.2. Secondary outcome measures

2.5.2.1. Inhibitory control. General response inhibition as well as response inhibition to food was measured using the Stop-Signal Task (SST; e.g., [29]). In the SST, participants performed a go task and a stop task. In the stop task, reactions to the go task had to be inhibited. The go stimuli in the general SST were the letters X and O; the go stimuli in the food SST were pictures of sweet and savoury food. The go stimulus was always presented for 1000 ms, and participants were required to respond as fast as possible to the stimulus by pressing response keys (e.g., press left for X/sweet and right for O/savoury). An auditory stop signal was presented on 25% of the trials, in which case participants were instructed not to respond to the stimulus. The delay between the go stimulus and stop signal was initially set at 250 ms and then dynamically adapted in order for participants to correctly inhibit 50% of the stop trials (the delay was increased when participants successfully inhibited their response, and the delay was decreased when participants failed to inhibit their response). For each SST (general and food-specific), participants completed practice blocks (40 trials in total) followed by two test blocks (64 trials each). The dependent measure was the stop-signal reaction time (SSRT), calculated by subtracting the mean stop delay from the mean reactions times. Higher SSRTs indicate worse inhibitory control. Poorer general and food-specific response inhibition (as measured by the SST) has been related to impulsivity and higher BMIs [29,33-35].

One to measure general response inhibition ability, and another to measure response inhibition specifically for food. In both SST tasks, the go stimulus was presented for 1000 ms, preceded by a 500 ms fixation cross. In the general SST, the go stimuli were the letters X and O. In the food specific SST, the go stimuli were four pictures of food (crisps, chocolate, party nuts, and chocolate chip cookies) in landscape or portrait format. During go trials, participants responded as fast as possible to the go stimulus using left and right response keys on the keyboard (e.g., press left for X [portrait] and right for O [landscape]). In both SST tasks, a visual stop signal was presented on 25% of the trails. Participants were instructed not to respond when this stop signal was presented. The delay between the go stimulus (X/O or food pictures) and the stop signal was initially set at 250 ms and was subsequently dynamically adapted using a tracking procedure to enable participants to correctly inhibit 50% of the stop trials: Following successful inhibition, the go–stop delay was increased by 50 ms. If participants failed to inhibit their response, the go–stop delay was decreased by 50 ms. Both SST variants consisted of one practice block without stop signals (10 trials), and one test block with stop signals (72 trials). The dependent variable, stop signal reaction time (SSRT), was calculated by subtracting the mean stop delay from mean reaction times. Higher SSRTs indicate decreased inhibitory control.

2.5.2.2. Self-control. Self-control was measured using the Self-Control Scale (SCS; [30]). The SCS is comprised of 36 items that are each scored on a 5-point scale. Higher scores indicate higher self-control. Evidence has been reported for the discriminant and convergent validity of the SCS [36,37].

2.5.2.3. Attentional bias to food cues. Attentional bias to food cues was measured using a visual probe task. Eye movements and manual response latencies were recorded as direct and indirect indices of attention allocation. Stimuli were pictures of highly palatable food items, musical instruments, and neutral non-food items. They were presented in pairs and presented next to each other during 2000 ms, followed by a probe in the location of one of the images. Participants were required to respond to the location of the probe by pressing a button. In critical trials, the stimulus pair consisted of a picture of food and a picture of a neutral instrument. Filler trials consisted of a pair of neutral pictures. In total, the task included 120 trials – 80 critical and 40 filler trials. Attention bias scores were derived from the eye movement data, and manual response latencies were based on response latencies to the location of the probes (see [31] for details). Evidence suggests that attention bias for food is causally related to eating behaviour [38].

2.5.3. Treatment mediators and moderators

2.5.3.1. Habituation of cue reactivity. In the cue exposure intervention only, self-reported desire to eat 100 mm VASs were used to assess within (WSH) and between-session habituation (BSH) of self-reported cue reactivity during cue exposure.

2.5.3.2. Expectancy violation. Eight CS-US expectancies were rated on perceived expectancy of a CS to be followed by the US using 100 mm VAS, a higher score reflecting a greater perceived expectancy. Items were formulated in "If CS then US" statements. Four CS-US expectancy items were standard for every participant, and four items were personalized based on the CS-US interview (see Table 2). CS-US expectancies have been assessed in previous cue exposure studies [14,39].

2.5.3.3. Sleep quality. The Pittsburgh Sleep Quality Index (PSQI; [32]) was used to measure sleep quality. The PSQI is a 19-item self-report measure that assesses several dimensions of sleep quality in the past month. Higher scores indicate poorer sleep quality.

Response inhibition, self-control, and attentional bias will also serve as moderators of treatment outcome.

Table 2
Overview of the eight CS-US expectancy items.

#	CS-US expectancy[a]
1.	If palatable food is in front of me, then I cannot refrain from eating it
2.	If (FF-list[b]) is in front of me, then I cannot refrain from eating it
3.	If I eat a small amount of (FF-list[b]), then I cannot stop eating
4.	If I eat a small amount of (FF-list[b]), then I cannot stop eating*
5.	Personalized CS-US expectancy 1[c]
6.	Personalized CS-US expectancy 2[c]
7.	If I eat a small amount of (FF-personal exposed[d]), then I cannot stop eating
8.	If I eat a small amount of (FF-personal exposed[d]), then I cannot stop eating*

On statements marked with *, participants took a small bite of the specific food before rating their expectancy.

[a] CS-US expectancy was scored on a VAS, and ratings ranged from 0 (not at all) to 100 (very strongly).

[b] 'FF-list' indicates the favourite food item selected from a list of ten snack foods.

[c] Personalized statements 5 and 6 are based on the CS-US interview (e.g., "If I feel exhausted and have excess to snack foods, then I will have a binge").

[d] 'FF-personal exposed' refers to a favourite personal snack food as assessed during the CS-US interview and utilized as exposed food item.

2.5.4. Treatment acceptability

Immediately after receiving the rationale of the intervention during the first therapy session, but prior to its start, participants were asked to rate their expectations of the intervention's effectiveness. Similar questions were administered after the intervention at post measurement: "*how appropriate will/was this intervention (be) for your complaints*"; "*how helpful will/was this intervention (be) in diminishing your complaints*"; "*would you recommend this intervention to a good friend?*" All items were rated on a 9-point scale from 1 (not at all) to 9 (very much).

3. Intervention

3.1. Therapists

Both interventions were delivered individually and conducted by PhD students and clinical psychology students who were obtaining their master degree. These students were not involved in the measurements. The therapists adhered to detailed study manuals, and received an extensive training for each intervention. Therapists participated in supervised meetings twice a week in order to discuss treatment progress and potential difficulties of individual participants. Sessions were audiotaped and listened to by the authors to ensure protocol adherence, and used for questions and feedback during the meetings.

3.2. Similarities of both interventions

Both interventions consisted of eight individual therapy sessions that took place during approximately one month (two sessions per week). In addition, all participants received psycho-education on the importance of good sleep quality for decreasing food consumption and BMI (e.g., [40]). Further, for all participants, unhealthy snacking behaviour was strongly discouraged: snacking should be kept to a minimum during the intervention period. Participants in both interventions also received homework, as specified below.

3.3. Cue exposure

The cue exposure intervention consisted of eight separate face-to-face sessions, and was designed according to the recommendations proposed by Craske et al. [18]. These techniques were translated to cue exposure as described in Table 3. A brief overview of the content of each exposure session is presented in Table 4. Next to the exposures during the therapy sessions, participants were instructed to do daily exposure exercises at home or other contexts. These homework exercises were prepared during the session with the therapist, and each completed exercise was registered. In case the participant would experience irresistible cravings at home and strongly believed she would engage in snacking behaviour (Section 3.2), she was instructed to follow a personal 'emergency card' that was composed together with the therapist in order to avoid unwanted reinforcement of existing CS-US associations. This was done by having the participant consume a different palatable food in an environment not previously associated with intake (e.g., the bathroom).

3.4. Lifestyle + control

The Lifestyle + intervention also consisted of eight sessions, including four face-to-face sessions (two at the university and two at the participant's home) that were alternated with four sessions via telephone. The basic components of the Lifestyle + intervention included

Table 3
Translation of the techniques as recommended by Craske et al. [18] to food cue exposure.

Technique	Translation
Expectancy violation	From the CS-US interview, the therapist received a report of the participant's favourite foods (USs) and food cues (CSs). Exposures were designed to maximally violate the personal CS-US expectancies: the therapist designed exposure exercises in a way that would maximize the perceived likelihood of the US to occur during exposure. Specific expectancies were assessed by the therapist before the start of exposure, and right after exposure to reflect on the discrepancy between what was expected and what was learned. *Example*: Lucy had the expectation to have a binge (US) when feeling exhausted and hungry after a stressful day of work and when high-calorie foods were in the cupboard (CSs). Exposures entailed feelings of exhaustion and hunger by planning the session after a long working day before dinner, and exposing Lucy to her specific binge food while smelling, touching, and licking it. The expectation of losing control was assessed before exposure, and the outcome (i.e., actual loss of control) was evaluated after the exercise.
Deepened extinction	Food cues were combined during cue exposure exercises after conducting exposure with at least one of the cues. During the first two exposure sessions, exposure exercises included more isolated CSs, such as the sight and smell of favourite food. From the third session on, additional relevant CSs were included. *Example*: Lucy was exposed in session one and two to chocolate of a specific brand, which was always part of her binge ritual. Exposure was conducted in a neutral laboratory: only smelling, touching and licking of the chocolate was part of the first two exposure sessions. From session three on, exposures took place in her living room, where additional CSs were carefully included during the exposure exercise, such as the sight and smell of different food items, the presence or absence of specific family members, and watching a specific TV show.
Multiple contexts	Exposure sessions took place in various external (e.g., the university, home environments, fast food restaurants) and internal (e.g., satiety) contexts. *Example*: After two exposure sessions in the laboratory, Lucy's sessions were planned at her home context, in her car after grocery shopping, and at the snack bar near her home. Further, exposures were done at varying levels of satiety (see Variability).
Occasional reinforced extinction	Participants occasionally took one bite of the food during exposure exercises. This occurred once every exposure session. *Example*: The therapist asked Lucy to take a small bite (i.e., a few grams) of the (binge) food at a random time-point during the exposure.
Removal of safety signals	Safety signals were identified and removed during the exposure sessions. *Example*: Lucy indicated that she would not lose control as long as the therapist was present. Therefore, during exposure sessions, the therapist sometimes left the room. In addition, exposure exercises were done at home without the presence of the therapist. Food for exposure exercises at home was at first provided by the therapist in a plastic container that Lucy needed to return on the next session, while during the course of therapy, Lucy bought her own food and practiced with her own plates, bowls, etc.
Variability	Level of satiety, type of food items, time of day, and length of the exposure sessions were measured and varied across sessions. *Example*: Lucy's exposures varied in length (between 5 min and 40 min), were planned on various times of day, and included various types of food items (e.g., chocolate bars, hamburgers, crisps). Over the sessions, it also became clear that Lucy's hunger was relatively stable on an intermediate level. To vary satiety levels, meals were planned right before or after the exposure sessions.
Retrieval cues	An instructional retrieval cue was used: participants were encouraged to mentally reinstate what was learned so far by writing down the main learning experiences and regularly rehearsing these outside the therapy sessions. This instructional retrieval cue was included from the third session on. *Example*: After completing the third session, Lucy wrote down her main learning experiences: she learned that she was able to control food intake, even in her 'weakest' moments when feeling exhausted, stressed and hungry. Further, she learned that food cravings eventually diminish without eating, which was in contrast to her expectation that only eating could relieve her cravings. She discussed her learning experiences with the therapist, and regularly read the assignment during the course of therapy.

Table 4
Short description of the content of the cue exposure and Lifestyle + control interventions, displayed per session (sessions 1 to 8).

	Cue exposure intervention*		Lifestyle + control intervention		
1	Context: Laboratory Techniques: • Expectancy violation • Deepened extinction • Occasional reinforced extinction Other: rationale, sleep quality, preparation emergency card and homework (exposures)	1	Context: Laboratory Content: • Dieting and healthy weight loss • Nutrients and energy balance • Satiety signals, tips to slow down eating • Mindfulness exercise Other: rationale, sleep quality, and preparation homework (energy balance and mindfulness)	5	Context: Home Content: • Media and thin-ideal • Body image and well-being • Mindfulness exercise • Q&A Other: Evaluation/preparation homework (thin-ideal and mindfulness)
2	Context: Laboratory Techniques: • Expectancy violation • Deepened extinction • Occasional reinforced extinction • Removal of safety signals Other: evaluation/preparation emergency card and homework (exposures)	2	Context: Phone Content: • Nutrients and energy balance • Q&A Other: Evaluation and preparation homework (energy balance and mindfulness)	6	Context: Phone Content: • Thin-ideal • Q&A Other: Evaluation/preparation homework (thin-ideal and mindfulness)
3–8	Context: Home and other relevant places Techniques: • Expectancy violation • Deepened extinction • Multiple contexts • Occasional reinforced extinction • Removal of safety signals • Variability • Retrieval cues (mental reinstatement) Other: evaluation/preparation emergency card and homework (exposures) *For a description of the exposure techniques, see Table 3.	3	Context: Laboratory Content: • Power-posing • Mindfulness exercise • Q&A Other: Evaluation/preparation homework (power-posing and mindfulness)	7	Context: Home Content: • Fat-talk and Photoshop • Body image and weight loss • Mindfulness exercise • Q&A Other: Evaluation/preparation homework (fat-talk and mindfulness
		4	Context: Phone Content: • Power-posing • Q&A Other: Evaluation/preparation homework (power-posing and mindfulness)	8	Context: Phone Content: • Fat talk • Q&A Other: Evaluation homework (fat-talk and mindfulness)

extensive healthy lifestyle advice, mindfulness, power-posing exercises (e.g., [41]), and psycho-education on body image (e.g., [42]). Table 4 provides a brief overview of the content of each session. Daily homework exercises consisted of mindfulness and an exercise related to the content of the previous session.

4. Statistical analyses

Weight change and expectancy violation at post-measurement and follow-up will be calculated by the change in percentage of weight/CS-US expectancy relative to pre-measurement. The mediating role of expectancy violation will be investigated by using the bootstrapping method as described by Preacher and Hayes [43]. Further, independent samples t-tests and repeated-measures ANOVAs will be used to examine the effects of treatment group on the other continuous outcome measures. The moderating role of habituation of desire to eat (WSH and BSH) on treatment outcome in the exposure intervention will be investigated using correlations. WSH will be operationalised by subtracting the end-level of desire to eat from the peak response of desire to eat during each session and averaging the scores for all sessions. BSH will be calculated by subtracting the peak response from session eight from the peak response of session one [19]. The other moderators of treatment outcome (change in inhibitory and self-control, attentional bias, and sleep quality) will be investigated using ANOVAs and correlational analyses. Lastly, associations between attentional bias and inhibitory and self-control will be examined using correlations.

5. Discussion

The main aim of this study was to examine the effects of a novel cue exposure intervention aimed at maximizing inhibitory learning, relative to an active control intervention. It was expected that participants assigned to the cue exposure vs. control intervention would lose more weight, show larger reductions in eating psychopathology and food cue reactivity, and consume less high-calorie snack foods, both at post-treatment and follow-up. As secondary aim, it was examined whether response inhibition, self-control, and attentional bias towards high-calorie foods showed greater reductions in the cue exposure vs. control intervention. It was further expected that treatment outcome would be mediated by increased CS-US expectancy violation, while habituation was not expected to play a role in treatment outcome. Finally, it was expected that treatment outcome was moderated by good sleep, high response inhibition and self-control, and low attentional bias towards high-calorie food.

The findings of the relatively few cue exposure studies that have been conducted are promising. However, these studies have often not examined weight loss, and some findings indicate returns of cravings and overeating at follow-up – suggesting cue exposure therapy still requires optimization (e.g., [10-15]). The present study attempts to address these issues by examining weight loss and by attempting to improve (long-term) outcomes. Specifically, we translated learning theory-based techniques proposed by Craske et al. [18] for the treatment of anxiety disorders to cue exposure therapy to reduce overeating and obesity, and tested the effectiveness of this inhibitory learning approach. The treatment was personalized for each participant: exposure exercises took place using the participant's CSs (physical contexts, times of day, mood, satiation states, presence or absence of family members) and USs (favourite high-calorie foods). Other notable strengths of the study are the inclusion of an active control treatment, a variety of measurements relevant to the study of overeating, an examination of underlying mechanisms, the use of experimenters who were blinded to the participant's condition, and only some drop-out ($n = 6$ after the start of the intervention). One limitation of the study is a limited sample size and power. In addition, it is not clear to what extent findings

generalize to male, under-aged and clinical samples. Nevertheless, the current paper provides a novel treatment protocol that can potentially improve current obesity treatments.

Conflict of interest

The authors report no conflict of interest.

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