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Modified Cue Exposure for Adolescents with Binge Eating Behaviour: Study Protocol of a Randomised Pilot Trial called $EXI_{(ea)}T$.

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Running Head: MODIFIED CUE EXPOSURE FOR ADOLESCENTS WITH BINGE EATING BEHAVIOUR

Abstract

Introduction: Binge eating (BE) behaviour is highly prevalent in adolescents, and can result in serious metabolic derangements and overweight in the long term. Weakened functioning of the behavioural inhibition system is one potential pathway leading to BE. Food cue exposure focusing on expectancy violation (CE_{EV}) is a short add-on intervention for BE that has proven effective in adults but has never been tested in adolescents. Thus, the current randomised pilot trial evaluates the feasibility of CE_{EV} for adolescents and its efficacy in reducing eating in the absence of hunger (EAH) of binge food items.

Methods and analysis: The trial will include *N* = 76 female adolescents aged between 13 and 20 years with a diagnosis of bulimia nervosa (BN), binge eating disorder (BED), or their subthreshold forms based on the DSM-5. Participants will be randomly assigned to two sessions of CE_{EV} or behavioural analysis (BA), a classical CBT-based intervention. The primary endpoint is the change in EAH measured according to ad libitum consumption of personally preferred binge food in a bogus taste test at post-test based on the intention-to-treat (ITT) population. Key secondary endpoints are changes in EAH of standardised binge food at post-test, in EAH at 3-month follow-up (FU), and in food craving after induction of food cue reactivity at posttest and FU. To identify further valid outcome parameters, we will assess effects of CE_{EV} compared to BA on global ED psychopathology, BE frequency within the last 28 days, body weight, response inhibition, and emotion regulation abilities. Treatment groups will be compared using analysis of covariance (ANCOVA) with intervention as fixed factor and BMI at baseline as covariate.

Ethics and dissemination: This clinical trial has been approved by the Ethics Review Committee of the Medical Association of Rhineland-Palatinate and the Medical Faculty of the Ruhr-University Bochum.

Strengths and limitations of this study

- The findings of $EXI_{(ea)}T$ will clarify the feasibility and efficacy of cue-exposure with expectancy violation (CE_{EV}) on ad libitum food intake and binge eating (BE) frequency in a transdiagnostic adolescent sample.
- $EXI_{(ea)}T$ is informed by previous evidence in adults and youth with obesity, includes age-appropriate material, and uses an objective measure as the primary outcome.
- $EXI_{(ea)}T$ is a randomised pilot trial comparing a short innovative add-on intervention comprising two sessions of CE_{EV} to behavioural analysis (BA) of BE episodes, the gold standard intervention of cognitive behaviour therapy (CBT).
- As a multicentre trial, $EXI_{(ea)}T$ enables a generalisation of the proof-of-concept, and contributes to quality assurance in the cooperating centres.
- Due to the short follow-up period of three months, we cannot draw any conclusions about the long-term efficacy of CE_{EV} for eating disorder psychopathology and body weight.

Protocol version 9.0, 25/07/2022

Trial registration: German Clinical Trials Register, DRKS00024009, 22/01/2021

INTRODUCTION

Binge eating in adolescents

Binge eating (BE) behaviour refers to recurrent episodes of impulsive overeating accompanied by the feeling of loss of control over eating. About 18% of 16-year-old adolescents reported BE as a single symptom at least sometimes, 8.5% even weekly during the last year.[1 2] BN is a core feature of both bulimia nervosa (BN) and binge eating disorder (BED), which show high prevalences of 0.9% to 3% (BN) and 1.32% to 5% (BED) in youth with overweight.[3 4 5] However, the majority of affected youth do not seek treatment as they associate BE with shame and guilt, leading to a long illness duration (8 to 14 years) and to a persistence of adverse outcomes into adulthood.[5 6]

Available first-line treatments for BE-related disorders in youth are mostly based on "enhanced" cognitive behaviour therapy for EDs (CBT-E).[7] Behavioural analysis (BA) of BE episodes is among the gold standard interventions within CBT-E, and focuses on early symptom changes.[8] CBT-E has been shown to be effective in achieving BE abstinence in almost 50% of patients with BN, but remission rates are lower in youth than in adults, e.g. 29% remitted.[9] Initial findings for CBT-E in adolescents with BED suggest that abstinence rates are comparable to those in adults, ranging between 43 and 61%.[10 11] Given the higher number of early responders in CBT-E compared to other therapy approaches, BA can be seen as at least partially responsible for the rapid therapeutic effects.[12 13]

In sum, at least 50% of youth continue to have BE episodes or certain impulsive eating behaviour patterns as residual symptoms at the end of treatment. One reason for this might be that the direct underlying mechanism - food-related inhibitory control deficits - is rarely targeted in conventional treatment programs.

Inhibitory control as an underlying mechanism

Recent studies emphasize an association of BE with self-reported impulsivity and behaviourally measured inhibitory control deficits.[14 15] Inhibitory control is conceptualised as the ability to inhibit impulsive responses in order to select a more value-based functional behaviour, e.g. eating out of deliberate pleasure instead of impulsivity.[16] Response inhibition in general, and towards food stimuli might be impaired in adults with bulimic-type EDs[17], although evidence for adolescents with BE is predominantly only available for non-clinical samples.[18 19] Moreover, a recent study

revealed that adolescents with obesity and BED displayed a poorer inhibition performance compared to normal-weight adolescents[20], although the study did not allow for any conclusions on stimulus specificity. Studies examining samples with overweight have yielded contradictory findings: While one study reported that children were less effective in food-specific response inhibition[21], we found that adolescent psychiatric inpatients showed a rather generally impaired inhibitory control irrespective of ED pathology.[22] Analogous to adults, it can be assumed that there is a specific subgroup of youth with impulsive eating patterns and inhibitory control deficits, presumably more generalised based on their current stage of development.

In this framework, the dual-pathway model by Hofmann and colleagues[23] postulates that BE is controlled via two processes - 1. automatic, unconscious processes and 2. reflexive, conscious processes. Automatic responses to food stimuli are primarily associated with the rewarding component of impulsive behaviour. This appetitive responding may be related to reward sensitivity and food-related inhibition deficits and is based on a heightened reactivity to palatable food cues or non-food cues that signal the availability of tempting food, i.e. food cue-reactivity.[24 25] In turn, top-down processes primarily involve executive functions such as emotion regulation and general inhibition abilities and are designed to counteract automatic behaviour.[26 27] A weakened reflexive system can be overridden by strong impulsive reactions to appetitive food stimuli, resulting in food craving and BE. Crucially, the impaired inhibitory control seems to be met with a hyperresponsive reward system due to neuroadaptive changes in reward circuits (see maintenance model for BE).[28]

In line with the dual-process model, recent findings have highlighted the interaction between emotion regulation and inhibitory control in terms of predicting BE.[29 30] In an adult sample with self-reported ED symptoms, eating expectancies mediated the relationship between emotion regulation difficulties and BE, but only in individuals with reward-based inhibition deficits.[30] Moreover, adolescents with poor self-reported inhibition experienced more uncontrolled eating, but only in the case of a negative mood.[31]

In sum, food-related inhibitory control deficits might act as an underlying perpetuating mechanism of BE, but studies examining interventions to address these deficits are lacking. So far, research has not identified an intervention for impulsive eating

behaviour that integrates food stimuli and has proven to be superior to other approaches.[10 32]

Inhibitory learning approach to exposure

One option to improve food-related inhibitory control is food cue exposure (CE), i.e. exposure to typical binge food and its stimulus characteristics, such as the taste or smell of a food, while preventing food consumption. The effect of CE on BE is often measured by the intake of palatable foods in laboratory paradigms, i.e. eating in the absence of hunger (EAH) in line with Birch and colleagues.[33]

Researcher have discussed two potential working mechanisms for CE in the area of BE: habituation and inhibitory learning. Initially, CE was seen as classical extinction training derived from principles of learning theory. Treatment manuals postulating habituation as a rationale recommend that patients focus on their desire to eat on a psychological and physiological level, while food stimuli (conditioned stimuli, CS) are presented in order to reduce food cue reactivity (conditioned appetitive responses, CR) via in-session habituation.[34] Since the 1980s, CE with habituation has mainly been researched for the treatment of BN, although over the years, this intervention was forgotten somewhat due to the complexity of implementing it in clinical practice.[35-38]

Recently, CE has been experiencing a revival in the treatment of BN and BED, with inhibitory control being used as rationale.[39-41] Research in anxiety disorders suggests that repeated exposure creates a new inhibitory association such that binge food then also signals the non-availability of the unconditioned eating response, i.e. a new CS-noUS pairing.[42] To enhance inhibitory learning in CE, sessions should be designed so as to maximize the discrepancy between the expectancy of overeating and what really happens, namely no overeating.[43] Magson and colleagues[44] even assume that habituation occurs because of inhibitory learning - if patients are exposed to food in such a way that their CS-US expectancies are not violated, no habituation processes will occur and they will be vulnerable to relapses. This assumption is also in line with observations that habituation within and between sessions, i.e. desire to eat, is not beneficially related to EAH and weight loss[39 43 45], whereas changes in expectancies were found to mediate treatment success regarding EAH.[43] Accordingly, CE should optimize the violation of idiographic beliefs about eating behaviour when confronted with the relevant binge food (e.g. “If I have milk chocolate next to me when I am sitting

alone doing my homework, I have to eat the whole bar."). In CE with expectancy violation (CE_{EV}), these beliefs are checked against what actually happens, i.e. the feared BE does not occur, which may strengthen the inhibitory pathway (e.g. "If I have milk chocolate […], I am able to resist eating the whole bar."). Moreover, possible underlying mechanisms of change such as inhibitory control and emotion regulation abilities will be altered due to their interactions with BE expectancies.[29-31]

Food cue exposure with expectancy violation influencing BE

A recent review[44] included 16 studies that investigated CE in adults with BE, three of which focused on expectancy violation.[39 43 45] Regardless of its focus, CE significantly reduced overeating expectancies, desire to eat, and EAH as measured by kcal consumption during a subsequent bogus taste test (BTT).[39] In addition, relative to a lifestyle intervention, CE_{EV} was more effective in reducing the number of BE episodes and also in reducing weight from baseline to 3-month follow-up (FU) in women with overweight (d = 0.67 and d = 0.65).[43] Moreover, EAH for exposed food decreased significantly in CE_{EV} (d = 0.35 – 0.81)[45], but this finding did not generalize to non-exposed food.[43] The opposite findings emerged for non-personalised exposed food items.[43 45] It can be suggested that personalised food items might better capture individual learning processes and should thus be included in CE in order to achieve more profound changes in food-related inhibitory control.

With regard to mechanisms of change, both generic and idiographic BE expectancies were found to be more effectively disconfirmed in $CE_{EV,}$ with d = 4.12 and d = 9.50, compared to active control interventions.[43 45] Moreover, in a recent within-group pilot study, significant improvements in expectancies about ability to tolerate distress were found after five sessions of CE_{EV} in women with BED.[46] Interestingly, expectancy violations (idiographic CS-US and distress tolerance expectancies) were found prior to changes in BE frequency, emphasizing their assumed potential for subsequent habituation processes.[44 46] To date, only one study has assessed self-reported impulsivity: Participants were randomized to an 8-session group intervention focusing on CE or a control intervention with both conditions including self-monitoring techniques.[40] No between-group differences emerged. To the best of our knowledge, however, no research has assessed the efficacy of CE for food-related inhibitory control and emotion regulation.

With respect to adolescent samples, CE has only been applied in two studies to date.[39 47] In patients with BN aged 14 to 19 years who had not responded well to CBT, a 12-session CE with habituation was effective in significantly decreasing BE and purging from baseline to post-treatment and at 6-month FU.[47] Schyns and colleagues[39] compared CE_{EV} with a lifestyle intervention in a clinical sample of adolescents with obesity. The main focus of the lifestyle intervention was on providing psychoeducation to increase healthier eating and physical activity. Two sessions of CE_{EV} were conducted and EAH was assessed as the primary endpoint, operationalised by the percentage of consumed kcal in a BTT relative to the personal daily energy requirement. CE_{EV} significantly reduced the ad libitum food intake of an exposed food item (chocolate mousse) and of non-exposed food items compared to the control condition (d = 0.80 and d = 0.76). Contrary to findings in adults, the exposure effects generalised to further highly palatable food, suggesting that adolescents might learn faster.[39] It can therefore be assumed that not all relevant food cues need to be integrated into CE_{EV} sessions. However, adherence to homework exercises was poor, suggesting the need for stronger guidance of CE_{EV} at home, especially in this young age group.

To sum up, evidence in adults and in adolescents with obesity indicates medium to large effect sizes regarding the improvement of EAH via ad libitum food intake, eating psychopathology, and weight reduction after only two sessions of CE_{EV}. However, more RCTs are needed to support this inhibitory learning approach to exposure in adolescents with BE.

STUDY AIMS AND HYPOTHESES

The current pilot study, called $EXI_{(ea)}T$, targets the feasibility and efficacy of CE_{EV} for adolescents with recurrent BE episodes relative to BA in a multicentre randomised trial. $EXI_{(ea)}T$ is an acronym for *EXIT* strategies as a way out of binge *ea*ting. Recurrent BE episodes are operationalised by a diagnosis of BN, BED, or Other Specified Feeding or Eating Disorder (OSFED-BN/BED).

Taken together, the aims of $EXI_{(ea)}T$ are to investigate (1) the application of CE_{EV} compared to BA in a transdiagnostic adolescent sample with BE, (2) whether CE_{EV} effectively reduces EAH and food craving at post-treatment and at 3-month FU, and (3) the effect of CE_{EV} on global ED pathology, number of binge episodes and weight,

and (4) on underlying mechanisms of change, i.e. expectancy violations. We hypothesize that CE_{EV} will be superior to BA in reducing ad libitum food intake of personally preferred exposed and non-exposed binge foods beyond physiological needs at post-test. With regard to secondary endpoints, we expect CE_{EV} to lead to a stronger decrease in ad libitum intake of standardised binge food, food craving, ED psychopathology, and BE frequency and to a stronger weight reduction at FU compared to BA. Moreover, we hypothesize that adolescents in the CE_{EV} condition will additionally benefit with respect to larger violations of BE expectancies. On an exploratory level, we will analyse potential moderating effects of food-related response inhibition and emotion regulation abilities.

METHODS AND ANALYSIS

Patient and Public Involvement

The modified CE was developed from clinical work with adolescents with EDs. To ensure appropriateness of CE_{EV} for the relevant clinical group and age range, a preliminary study was conducted with a student sample aged 18-25 years who experienced stress-induced chocolate cravings. The results of this preliminary study on treatment expectations were used to optimise the CE before inclusion of the first patient.

Study design

This study is a randomized (with a 4:4 allocation ratio), controlled, double-blind multicentre trial comparing CE_{EV} to BA. Recruitment, data collection, interventions and data analysis are conducted in two departments of child and adolescent psychiatry and psychotherapy at the University Hospital Bochum and the University Medical Center Mainz.

Participants and recruitment

The following inclusion criteria are applied 1) female adolescents aged 13;00 to 20;11 years; 2) presence of recurrent BE episodes (at least three objective episodes within the last three months with loss of control and clinically significant distress/functional impairment) assessed via an expert interview (Eating Disorder Examination, EDE-II[48 49]); 3) diagnosis of BN, BED or OSFED-BN/BED (BN or BED of low frequency and/or

limited duration) based on DSM-5; 4) sufficient knowledge of the German language; and 5) written informed consent of the participant and the caregivers. Adolescents are excluded if they show 1) severe psychopathological comorbidities (such as severe depressive episodes, borderline personality disorder, substance use disorder, dissociative disorders, diagnosis of non-suicidal self-injury based on DSM-5), although mild to moderate comorbidities do not lead to exclusion as long as ED symptoms are the core symptoms; 2) anorexia nervosa; 3) immediate need for inpatient treatment due to acute suicidality or BE/purging at a high frequency; and 4) ongoing outpatient treatment with a focus on ED-specific interventions (e.g. CE, mirror exposure). The participants are recruited via press releases, flyers, and social media, as well as in schools, and youth centres in Hamm and Mainz and the surrounding areas. In addition, cooperations with counselling centres, child and adolescent psychiatrists and psychotherapists, and pediatricians are used for recruitment.

Study flow and procedure

The study flow is illustrated in Fig. 1. First, subjects and their caregivers are informed about the aims and procedure of the study in a telephone interview (T_0). In addition, the inclusion and exclusion criteria are checked.

Please insert Figure 1 here.

At the beginning of each session, participants` most recent food intake is assessed and their current levels of hunger and desire to eat are measured on a 100mm visual analogue scale (VAS). At the baseline assessment (T_1), participants undertake two computer-based tasks (Food Craving Task, FCT[50]; Go/NoGo Task, GNG[51 52]), before their weight, height and body fat percentage are measured by bioelectrical impedance analysis (BIA). Moreover, general psychopathology is assessed and the EDE-II and an interview on binge food (in which participants are asked to state four personally preferred binge foods) are conducted. After a short break, relevant parts of the Diagnostic Interview for Mental Disorders in Children and Adolescents (Kinder-DIPS-OA)[53] are conducted. The remaining self-rating questionnaires are completed online via REDCap[54]. The randomisation takes place after T_1 using a blockwise procedure (block sizes of four). To ensure that assessors (experienced and trained psychologists)

are blinded, the study leaders randomize the participants. Two sessions of CE_{EV} or BA follow at T_2 and T_3. Participants are requested to eat sufficiently prior to the appointments but not within the last two hours before the intervention. To avoid hunger during the interventions, participants are asked to eat a cereal bar 15 minutes before the intervention. After CE_{EV} and BA, current levels of hunger, desire to eat, and the two relevant overeating expectancies in the CE_{EV} group are assessed again. At the end of the intervention sessions, participants are strongly encouraged to repeat the exercise at home to increase the transferability to daily life. We look for specific favourable times of day for the implementation and anticipate possible difficulties or obstacles. The participants also receive an exercise booklet with general information about the intervention as well as detailed instruction and protocol sheets. At the beginning of T_3, these home exercises, obstacles to implementation and potential solutions are discussed and participants are again encouraged to continue with the exercises at home. At the end of T_3, a BTT with all four preferred binge foods is conducted.

At the post-assessment (T_4), the frequency of home exercises is discussed again. Next, a BTT is performed with standardised non-exposed food items (milkshakes), and the computer-based tasks are repeated. Binge-purge behaviours are assessed. The questionnaires can be completed at home. The post-assessment is repeated at T_5 (FU) three months after T_4. At T_5, the BTT is conducted with three preferred and one standardised binge foods. Any outstanding questionnaires are completed on site to avoid missing data. At the end of T5, participants receive an allowance of 50€.

Interventions

Both conditions include two face-to-face sessions with a maximum duration of 70 minutes each. Following a standardised session protocol (see Supplement), the interventions are delivered by experienced CBT therapists at each site. In the CE_{EV} group, participants are exposed to two out of four personally preferred binge food items. Two individual overeating expectancies are used during exposure, and if a subject has difficulties in formulating expectancies, standardised overeating expectances are applied (i.e. “If I see delicious food, I won’t be able to resist eating it.”). Directly before CE_{EV} and every five minutes, subjects are asked to rate their current levels of hunger, desire to eat the exposed food, and the two relevant overeating expectancies on a 100mm VAS. The exposure ends as soon as the desire to eat has decreased by 50%

compared to the highest rating, but at the latest after 70 minutes. After the exposure, two alternative, helpful expectancies are developed together with the therapist and are written on two index cards so that the participant can carry them with her. Control group participants undergo a BA of the last BE episode based on the SORKC model.[55] First, situational and preceding factors as well as the cognitive, emotional, physiological and behavioural reactions of the participant are identified. In addition, consequences of the behaviour are detected. The BA ends with a solution analysis by identifying effective skills to prevent BE, but also after 70 minutes at the latest.

Diagnostic and outcome assessments

Patient characteristics and diagnostics

Besides sociodemographic information such as age and school type, general information such as ongoing therapy, and previous treatments is gathered. In addition, information to compute the socioeconomic status (SES; Winkler-Index[56]) is obtained. To identify possible comorbidities, the Freiburger Screening for Mental Disorders (FSP)[57] is used as screening instrument. The sections on depressive disorders, anxiety disorders, ADHD, conduct disorders, tic disorders, enuresis, encopresis and non-suicidal self-injury disorder are administered routinely in the Kinder-DIPS-OA; the other sections are explored in the case of relevant answers in the previously administered FSP. Eating disorder psychopathology is assessed with the well-established interview EDE-II which allows an accurate clinical judgment of global ED psychopathology over the last 28 days and is considered the gold standard for ED-specific diagnostics.[58] Other diagnostics are general psychopathology[59 60], last food intake, level of hunger and desire to eat. Instruments and their psychometric characteristics are illustrated in Table 1.

Table 1. Assessment plan from screening (T_0) to 3-month follow-up (T_5).

Variable	Instrument	Description	Score indication	Assessment moments				
				T_1	T_2	T_3	T_4	T_5
Diagnostics								
Eligibility screen		Inclusion and exclusion criteria		X				
Clinical baseline data		e.g. age, school type, treatments		X				
General psychopathology - self-report	Strengths and Difficulties Questionnaire (SDQ)[59 60]	25 items range from 0-40	Higher scores indicate more externalising and internalising problems	X				
Psychological impairment	Freiburger Screening für psychische Störungen (FSP)[57]	Screening questions for 14 mental disorders with 29 items		X				
General psychopathology - clinical judgment	Diagnostic Interview for Mental Disorders in Children and Adolescents (Kinder-DIPS-OA)[53]	Screening for mental disorders according to the DSM-IV-TR[54] and ICD-10[55]		X				
Eating disorder psychopathology - clinical judgment	Eating Disorder Examination-II (EDE-II)[48 49]	Semi-structured interview with 22 and four subscales “Restraint”, “Eating concerns”, Shape concerns”, and “Weight concerns”	Higher scores indicate more eating disorder psychopathology	X				
Primary outcome								
Eating in the absence of hunger (EAH)	Bogus Taste task (BTT, preferred food items)[61]	Exposition to their personally preferred food items	Higher consumed calories indicate more EAH			X		X
Secondary outcomes								
Eating in the absence of hunger (EAH)	Bogus Taste task (BTT, standardised food items)[66]	Exposition to milkshakes	Higher consumed calories indicate more EAH				X	X
Momentary food craving	Food Challenge Task (FCT)[50]	Craving is measured with the Food Craving Questionnaire-	Higher scores indicate higher intensity of craving	X			X	X

		State (FCQ-S)[63 64], consists of 15 items range from 15-75				
Binge eating	Eating Disorder Examination-II (EDE-II)[48 49]			X	X	X
Eating disorder psychopathology - self-report	Eating Disorder Examination-Questionnaire (EDE-Q)[65 66]	Self-report questionnaire with 22 items	Higher scores indicate more eating disorder psychopathology	X	X	X
Weight, height, body fat	Bioelectrical impedance analysis (BIA), InBody770*			X	X	X
Food craving	Food Craving Questionnaire-Trait (FCQ-T-r)[63 67]	15 items range from 15-90	Higher scores indicate higher frequency and intensity of food craving	X	X	X
Moderator variables						
Response inhibition	Go/NoGo Task (GNG Task)[51 52]	Affective shifting task with high-caloric vs. neutral food stimuli; 16 blocks with a total of 320 trials	Higher number of commission errors indicate lower inhibition skills	X	X	X
Emotion regulation	Difficulties in Emotion Regulation Scale (DERS)[68 69]	36 items range from 36-180	Higher scores indicate more difficulties in emotion regulation	X	X	X
Treatment expectation and evaluation						
Treatment expectation	Expectation of Improvement and Suitability of Treatment Form (EIST)[76]	Two items, rated on a 10-point Likert scale	Higher scores indicate positive treatment expectation	X	X	X
Treatment evaluation	Patient Questionnaire on Therapy Expectation and Evaluation (PATHEV)[78]	11 items, rated on a 5-point Likert scale	Higher score indicate better treatment evaluation	X	X	X

Notes. T_0 = Telephone interview; T_1 = Baseline assessment; T_2 = Intervention session 1; T_3 = Intervention session 2; T_4 = Post-assessment; T_5 = Follow-up; * Body fat is only measured at the Mainz site.

Primary Outcome

EAH is assessed with BTT, a valid and sensitive instrument to investigate whether experimental manipulations affect food intake.[61] Participants are exposed to their personally preferred binge foods and are asked to evaluate the taste of the food on a rating sheet. They are invited to eat as much as they need to evaluate the taste. Before and after the rating, the weight of the food is measured and the consumed calories are calculated. The dependent variable is the percentage of consumed calories in relation to the individual's daily energy requirements with respect to age and gender in line with the recommendations of the United Nations University and the World Health Organization.[62]

Secondary Outcomes

EAH is measured with standardized food items in the BTT. Momentary food craving is assessed with the FCT in which a five-minute video with tasty foods is presented to induce craving. After participants have watched the video, the experience of craving is measured with the Food Craving Questionnaire-State (FCQ-S).[63] [64] The FCT has proven to be valid for the standardised induction of food cue reactivity to measure momentary food craving.[50] Other secondary outcome measures are binge eating, eating disorder psychopathology[65] [66], weight, height, body fat and trait food craving (FCQ-T-r).[63] [67]

Moderators

To identify possible moderating effects, emotion regulation is measured with the Difficulties in Emotion Regulation Scale (DERS)[68] [69], and response inhibition is assessed with a modified personalised GNG affective shifting task (high-calorie food category vs. neutral category).[51] [52] Neutral stimuli (flower, towel) and high-calorie foods (chocolate, pizza) are presented as Go or NoGo stimuli (depending on the block). To determine participants` personal taste preferences, prior to the GNG Task, they are asked to rate 30 high-calorie food stimuli on a 7-point Likert scale (0 = not at all palatable to 6 = extremely palatable). The ten personally most palatable food stimuli are then used in the task. Participants are instructed to press a button when watching a relevant stimulus ("Go") and to not press the button when watching an irrelevant stimulus ("NoGo"). The task consists of 16 blocks with 50% of the stimuli presented as Go stimuli and 50% as NoGo stimuli in each block. Participants receive instructions at

the beginning of each block. Each stimulus is presented for 500ms with an inter-trial interval of 1000ms. Dependent variables are participants` reaction times and number of commission errors (false reactions to a NoGo instruction) and omission errors (missing reactions to a Go instruction). The GNG task is a widely used task to measure response inhibition.[22]

Additional assessments

Adherence control

Attrition rate and study dropouts are assessed in both treatment groups. Manual adherence across the different therapists is achieved through standardised treatment protocols, online trainings and fortnightly supervisions by a licensed expert in ED treatment (TL) across both participating centres.

Treatment Expectation and Evaluation

Treatment expectation and evaluation are assessed with the Expectation of Improvement and Suitability of Treatment Form (EIST)[76] and the Patient Questionnaire on Therapy Expectation and Evaluation (PATHEV).[78]

Sample size calculation

The sample size calculation is based on the publication of Schyns and colleagues[39], which reports an effect size of d = 0.8 between groups for the percentage of consumed kcal during the taste test relative to the daily energy requirements (experimental group: mean 57% (N = 21; SD = 68%), control group: mean 146% (N = 19; SD = 141%)). When calculating the pooled standard deviation (SD_{pooled} = 118.5%) and assuming an effect size of 0.8, this results in an absolute difference of 75% in the mean between groups, which can be considered as relevant. When assuming a two-sided significance level, a power of 90%, an effect size of d = 0.8, and a sample size of 68 patients (=2x34 patients) will be needed to detect a significant treatment difference at post-assessment when using a t-test. As the duration of treatment is very short (two weeks only), we assume that patient loss due to non-compliance will be minimal. To account for 10% dropouts[39], 76 patients should be randomised. The calculation was performed using SAS Version 9.4.

Data analysis plan

Regarding the primary outcome EAH, treatment groups will be compared using an analysis of covariance (ANCOVA) with intervention as fixed factor and BMI at baseline as covariate. The primary analysis is performed on the ITT population consisting of all patients randomised. The secondary parameters are mostly continuous parameters, and will be analysed using AN(C)OVAs and t-tests. Sample characteristics will be provided. A p-value of < .05 is considered as statistically significant (two-sided). Missing values will not be replaced. There will be several sensitivity analyses, e.g. by considering additional covariates.

ETHICS AND DISSEMINATION

Ethics and safety aspects

The trial will be conducted according to the principles of ICH-GCP and appropriate legal regulations, and will be adhere to the Declaration of Helsinki in its latest version. Participating individuals are provided with treatment as usual (TAU which consists of BA) for EDs according to good clinical practice.[70] The study protocol including amendments has been and will be approved by the responsible ethics committees. Important protocol modifications will be reported to the German Clinical Trials Register and to the journal. Participants and caregivers must provide written informed consent before beginning the study. CE is generally well tolerated[39 43], and risks for participants are not known or expected. Trained clinical staff will be available to monitor safety concerns and support patients during/after treatment.

Dissemination plan

The collected data will be published in relevant scientific journals and will be presented at conferences. Participants data will only be published in anonymised form.

DISCUSSION

Research on add-on treatment elements for BE in adolescents is still limited, leaving a gap in knowledge on interventions that might enhance outcomes for this age group. One promising way to achieve this might be to target food-related inhibitory control as

an underlying perpetuating mechanism of BE. Recent results suggest a successful adaptation of CE_{EV} for pathological eating behavior. However, little is known about the feasibility and efficacy of CE_{EV} for adolescents with recurrent BE episodes. Thus, the findings of $EXI_{(ea)}T$ might clarify whether CE_{EV} is accepted by a transdiagnostic adolescent sample and whether it is able to reduce the ad libitum consumption of highly palatable foods when satiated as well as ED pathology. Furthermore, we will elucidate the role of CS-US expectancy violations, response inhibition, and emotion regulation in $CE_{EV.}$ The strengths of $EXI_{(ea)}T$ lie in the inclusion of a credible, active control condition, considered as the gold standard intervention of CBT-E to treat BE, and the use of an objective measure to assess changes, i.e. ad libitum food intake, as the primary efficacy endpoint. Moreover, the CE_{EV} treatment protocol includes the most relevant CE strategies to maximize treatment success[44], i.e. in-vivo exposure, personally preferred food cues and non-food cues (due to imagery of trigger situations at the beginning of session), occasionally eating allowed and personal CS-US expectancies identified. Additionally, to overcome poor homework adherence, we offer a detailed exercise booklet, discuss implementation problems and debrief all exercises at the beginning of session 2. On the level of limitations, it should be noted that $EXI_{(ea)}T$ cannot evaluate the efficacy of CE_{EV} as an add-on intervention to CBT-E as a whole. Moreover, there is no data monitoring committee to review accumulating data, which may affect the independence of the analyses. In addition, our decision to use the DSM-5 criteria and not the age-adapted criteria for BED[71 72] or modified ICD-11 criteria for bulimic disorders[73], which emphasize the subjective loss of control (LOC), needs to be explored with respect to recruitment procedures. Indeed, we have not found prior evidence that CE_{EV} is also a valuable intervention with respect to LOC eating.

However, if CE_{EV} is effective and feasible for adolescents with BE, we might conduct a confirmatory randomised trial in order to test CE_{EV} as a useful adjunct to first-line treatment.

Trial status

Recruitment for this trial started in April 2021 and is ongoing.

Contributions

All authors contributed to the design and conception of this study. HP, IK, JE and TL elaborated the study protocol and gained ethical approval. HP and IK drafted the manuscript and all co-authors revised the manuscript critically. All authors have read and approved the final version of the article submitted.

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Competing interests

TL receives royalties for textbooks in the field of eating disorders from Hogrefe, Kohlhammer, Springer and DeGruyter as well as funding from the German Ministry of Education and Research (BMBF) for studies in the field of eating disorders and obesity. HP receives royalties for a therapy manual for BE from Hogrefe. The other authors declare that they have no competing interests.

Ethics approval

Ethical approval has been granted by the Ethics Review Committee of the Medical Association of Rhineland-Palatinate (No. 2020-14980) and of the Medical Faculty of the Ruhr-University Bochum (No. 20-7051 BR).

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES

1. Olsen EM, Koch SV, Skovgaard AM, et al. Self-reported symptoms of binge-eating disorder among adolescents in a community-based Danish cohort-A study of prevalence, correlates, and impact. *Int J Eat Disord* 2021;54(4):492-505. doi: 10.1002/eat.23458
2. Flament MF, Henderson K, Buchholz A, et al. Weight Status and DSM-5 Diagnoses of Eating Disorders in Adolescents From the Community. *J Am Acad Child Adolesc Psychiatry* 2015;54(5):403-11 e2. doi: 10.1016/j.jaac.2015.01.020
3. Campbell K, Peebles R. Eating disorders in children and adolescents: state of the art review. *Pediatrics* 2014;134(3):582-92. doi: 10.1542/peds.2014-0194
4. Kjeldbjerg ML, Clausen L. Prevalence of binge-eating disorder among children and adolescents: a systematic review and meta-analysis. *Eur Child Adolesc Psychiatry* 2021 doi: 10.1007/s00787-021-01850-2
5. Marzilli E, Cerniglia L, Cimino S. A narrative review of binge eating disorder in adolescence: prevalence, impact, and psychological treatment strategies. *Adolesc Health Med Ther* 2018;9:17-30. doi: 10.2147/AHMT.S148050
6. Goldschmidt AB, Wall MM, Loth KA, et al. The course of binge eating from adolescence to young adulthood. *Health Psychol* 2014;33(5):457-60. doi: 10.1037/a0033508
7. Mulkens S, Waller G. New developments in cognitive-behavioural therapy for eating disorders (CBT-ED). *Curr Opin Psychiatry* 2021;34(6):576-83. doi: 10.1097/YCO.0000000000000745
8. Fairburn CG. Cognitive behaviour therapy and eating disorders.: Guilford Press 2008.
9. Gorrell S, Matheson BE, Lock J, et al. Remission in adolescents with bulimia nervosa: Empirical evaluation of current conceptual models. *Eur Eat Disord Rev* 2020;28(4):445-53. doi: 10.1002/erv.2729
10. Hilbert A, Petroff D, Neuhaus P, et al. Cognitive-Behavioral Therapy for Adolescents with an Age-Adapted Diagnosis of Binge-Eating Disorder: A Randomized Clinical Trial. *Psychother Psychosom* 2020;89(1):51-53. doi: 10.1159/000503116
11. Hilbert A, Petroff D, Herpertz S, et al. Meta-analysis on the long-term effectiveness of psychological and medical treatments for binge-eating disorder. *Int J Eat Disord* 2020;53(9):1353-76. doi: 10.1002/eat.23297
12. Linardon J, Brennan L, de la Piedad Garcia X. Rapid response to eating disorder treatment: A systematic review and meta-analysis. *Int J Eat Disord* 2016;49(10):905-19. doi: 10.1002/eat.22595
13. Fairburn CG, Bailey-Straebler S, Basden S, et al. A transdiagnostic comparison of enhanced cognitive behaviour therapy (CBT-E) and interpersonal psychotherapy in the treatment of eating disorders. *Behav Res Ther* 2015;70:64-71. doi: 10.1016/j.brat.2015.04.010
14. Giel KE, Teufel M, Junne F, et al. Food-Related Impulsivity in Obesity and Binge Eating Disorder-A Systematic Update of the Evidence. *Nutrients* 2017;9(11) doi: 10.3390/nu9111170
15. Schag K, Schonleber J, Teufel M, et al. Food-related impulsivity in obesity and binge eating disorder--a systematic review. *Obes Rev* 2013;14(6):477-95. doi: 10.1111/obr.12017

16. Verbruggen F, Logan GD. Automatic and controlled response inhibition: associative learning in the go/no-go and stop-signal paradigms. *J Exp Psychol Gen* 2008;137(4):649-72. doi: 10.1037/a0013170
17. Wu MD, Hartmann M, Skunde M, et al. Inhibitory Control in Bulimic-Type Eating Disorders: A Systematic Review and Meta-Analysis. *Plos One* 2013;8(12) doi: ARTN e8341210.1371/journal.pone.0083412
18. Ames SL, Kisbu-Sakarya Y, Reynolds KD, et al. Inhibitory control effects in adolescent binge eating and consumption of sugar-sweetened beverages and snacks. *Appetite* 2014;81:180-92. doi: 10.1016/j.appet.2014.06.013
19. Byrne ME, Shank LM, Altman DR, et al. Inhibitory control and negative affect in relation to food intake among youth. *Appetite* 2021;156:104858. doi: 10.1016/j.appet.2020.104858
20. Kittel R, Schmidt R, Hilbert A. Executive functions in adolescents with binge-eating disorder and obesity. *Int J Eat Disorder* 2017;50(8):933-41. doi: 10.1002/eat.22714
21. Nederkoorn C, Coelho JS, Guerrieri R, et al. Specificity of the failure to inhibit responses in overweight children. *Appetite* 2012;59(2):409-13. doi: 10.1016/j.appet.2012.05.028
22. Deux N, Schlarb AA, Martin F, et al. Overweight in adolescent, psychiatric inpatients: A problem of general or food-specific impulsivity? *Appetite* 2017;112:157-66. doi: 10.1016/j.appet.2017.01.031
23. Hofmann W, Friese M, Strack F. Impulse and Self-Control From a Dual-Systems Perspective. *Perspect Psychol Sci* 2009;4(2):162-76. doi: 10.1111/j.1745-6924.2009.01116.x
24. Jansen A, Schyns G, Bongers P, et al. From lab to clinic: Extinction of cued cravings to reduce overeating. *Physiol Behav* 2016;162:174-80. doi: 10.1016/j.physbeh.2016.03.018
25. van den Akker K, Stewart K, Antoniou EE, et al. Food Cue Reactivity, Obesity, and Impulsivity: Are They Associated? *Current Addiction Reports* 2014;1(4):301-08. doi: 10.1007/s40429-014-0038-3
26. Legenbauer T, Preuss H. Improving Impulse and Emotion Regulation in Binge Eating Disorder: Possible Application and First Results of the ImpulsE Manual. *Kindh Entwickl* 2019;28(4):210-19. doi: 10.1026/0942-5403/a000292
27. Preuss H, Leister L, Pinnow M, et al. Inhibitory control pathway to disinhibited eating: A matter of perspective? *Appetite* 2019;141:104297. doi: 10.1016/j.appet.2019.05.028
28. Treasure J, Leslie M, Chami R, et al. Are trans diagnostic models of eating disorders fit for purpose? A consideration of the evidence for food addiction. *Eur Eat Disord Rev* 2018;26(2):83-91. doi: 10.1002/erv.2578
29. Van Malderen E, Goossens L, Verbeken S, et al. The interplay between self-regulation and affectivity in binge eating among adolescents. *Eur Child Adolesc Psychiatry* 2019;28(11):1447-60. doi: 10.1007/s00787-019-01306-8
30. Smith KE, Mason TB, Peterson CB, et al. Relationships between eating disorder-specific and transdiagnostic risk factors for binge eating: An integrative moderated mediation model of emotion regulation, anticipatory reward, and expectancy. *Eat Behav* 2018;31:131-36. doi: 10.1016/j.eatbeh.2018.10.001
31. Van Malderen E, Kemps E, Verbeken S, et al. Food for mood: Experimentally induced negative affect triggers loss of control over eating in adolescents with low inhibitory control. *Int J Eat Disord* 2021;54(3):388-98. doi: 10.1002/eat.23422

32. Ince B, Schlatter J, Max S, et al. Can we change binge eating behaviour by interventions addressing food-related impulsivity? A systematic review. *J Eat Disord* 2021;9(1):38. doi: 10.1186/s40337-021-00384-x
33. Birch LL, Fisher JO, Davison KK. Learning to overeat: maternal use of restrictive feeding practices promotes girls' eating in the absence of hunger. *Am J Clin Nutr* 2003;78(2):215-20. doi: 10.1093/ajcn/78.2.215
34. Jansen A, Van den Hout MA, De Loof C, et al. A case of bulimia successfully treated by cue exposure. *J Behav Ther Exp Psychiatry* 1989;20(4):327-32. doi: 10.1016/0005-7916(89)90064-5
35. Fairburn C. A cognitive behavioural approach to the treatment of bulimia. *Psychol Med* 1981;11(4):707-11. doi: 10.1017/s0033291700041209
36. Leitenberg H, Gross J, Peterson J, et al. Analysis of an Anxiety Model and the Process of Change during Exposure Plus Response Prevention Treatment of Bulimia Nervosa. *Behav Ther* 1984;15(1):3-20. doi: 10.1016/S0005-7894(84)80038-6
37. Jansen A, Broekmate J, Heymans M. Cue-exposure vs self-control in the treatment of binge eating: a pilot study. *Behav Res Ther* 1992;30(3):235-41. doi: 10.1016/0005-7967(92)90069-s
38. Rosen JC, Leitenberg H. Bulimia nervosa: Treatment with exposure and response prevention. *Behav Ther* 1982;13(1):117-24. doi: 10.1016/S0005-7894(82)80055-5
39. Schyns G, Roefs A, Smulders FTY, et al. Cue exposure therapy reduces overeating of exposed and non-exposed foods in obese adolescents. *J Behav Ther Exp Psychiatry* 2018;58:68-77. doi: 10.1016/j.jbtep.2017.09.002
40. Schag K, Rennhak SK, Leehr EJ, et al. IMPULS: Impulsivity-Focused Group Intervention to Reduce Binge Eating Episodes in Patients with Binge Eating Disorder - A Randomised Controlled Trial. *Psychother Psychosom* 2019;88(3):141-53. doi: 10.1159/000499696
41. Ferrer-Garcia M, Pla-Sanjuanelo J, Dakanalis A, et al. Eating behavior style predicts craving and anxiety experienced in food-related virtual environments by patients with eating disorders and healthy controls. *Appetite* 2017;117:284-93. doi: 10.1016/j.appet.2017.07.007
42. Craske MG, Treanor M, Conway CC, et al. Maximizing exposure therapy: An inhibitory learning approach. *Behaviour Research and Therapy* 2014;58:10-23. doi: 10.1016/j.brat.2014.04.006
43. Schyns G, van den Akker K, Roefs A, et al. Exposure therapy vs lifestyle intervention to reduce food cue reactivity and binge eating in obesity: A pilot study. *J Behav Ther Exp Psychiatry* 2020;67:101453. doi: 10.1016/j.jbtep.2019.01.005
44. Magson NR, Handford CM, Norberg MM. The Empirical Status of Cue Exposure and Response Prevention Treatment for Binge Eating: A Systematic Review. *Behav Ther* 2021;52(2):442-54. doi: 10.1016/j.beth.2020.06.005
45. Schyns G, Roefs A, Mulkens S, et al. Expectancy violation, reduction of food cue reactivity and less eating in the absence of hunger after one food cue exposure session for overweight and obese women. *Behav Res Ther* 2016;76:57-64. doi: 10.1016/j.brat.2015.11.007
46. Norberg MM, Handford CM, Magson NR, et al. Reevaluating Cue Exposure and Response Prevention in a Pilot Study: An Updated Treatment for Binge Eating Disorder. *Behav Ther* 2021;52(1):195-207. doi: 10.1016/j.beth.2020.04.003

47. Martinez-Mallen E, Castro-Fornieles J, Lazaro L, et al. Cue exposure in the treatment of resistant adolescent bulimia nervosa. *Int J Eat Disord* 2007;40(7):596-601. doi: 10.1002/eat.20423
48. Fairburn CG, Cooper Z. The Eating Disorder Examination (12th edition). In: Fairburn CG, Wilson GT, eds. 12th edition ed: Guilford Press 1993:317–60
49. Hilbert A, Tuschen-Caffier B. Eating Disorder Examination-II: Deutschsprachige Übersetzung (2. Auflage): Tübingen: dgvt-Verlag 2016.
50. Van den Eynde F, Claudino AM, Mogg A, et al. Repetitive transcranial magnetic stimulation reduces cue-induced food craving in bulimic disorders. *Biol Psychiatry* 2010;67(8):793-5. doi: 10.1016/j.biopsych.2009.11.023
51. Meule A, Kubler A. Double trouble. Trait food craving and impulsivity interactively predict food-cue affected behavioral inhibition. *Appetite* 2014;79:174-82. doi: 10.1016/j.appet.2014.04.014
52. Meule A, Lutz AP, Krawietz V, et al. Food-cue affected motor response inhibition and self-reported dieting success: a pictorial affective shifting task. *Front Psychol* 2014;5:216. doi: 10.3389/fpsyg.2014.00216
53. Schneider S, Pflug V, In-Albon T, et al. Kinder-DIPS Open Access: Diagnostisches Interview bei psychischen Störungen im Kindes-und Jugendalter 2018.
54. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208
55. Kanfer FH, Philips JS. Lerntheoretische Grundlagen der Verhaltenstherapie. München: Kindler 1970.
56. Winkler J, Stolzenberg H. Adjustierung des Sozialen-Schicht-Index für die Anwendung im Kinder- und Jugendgesundheitssurvey (KiGGS). Wismarer Diskussionspapiere. Wismar: Hochschule Wismar, Fakultät für Wirtschaftswissenschaften, 2009.
57. Hölzel, Ower, Berger, et al. FSP - Freiburger Screening für Psychische Störungen nach ICD-10 [in preparation]. Kurzzeitbehandlung bei psychischen Störungen in der Hausarztpraxis: Elsevier-Verlag.
58. Berg KC, Peterson CB, Frazier P, et al. Psychometric evaluation of the eating disorder examination and eating disorder examination-questionnaire: a systematic review of the literature. *Int J Eat Disord* 2012;45(3):428-38. doi: 10.1002/eat.20931
59. Goodman R, Meltzer H, Bailey V. The Strengths and Difficulties Questionnaire: a pilot study on the validity of the self-report version. *Eur Child Adolesc Psychiatry* 1998;7(3):125-30. doi: 10.1007/s007870050057
60. Lohbeck A, Schultheiss J, Petermann F, et al. The German Self-Report Version of the Strengths and Difficulties Questionnaire (SDQ-Deu-S): Psychometric Properties, Factor Structure, and Critical Values. *Diagnostica* 2015;61(4):222-35. doi: 10.1026/0012-1924/a000153
61. Robinson E, Haynes A, Hardman CA, et al. The bogus taste test: Validity as a measure of laboratory food intake. *Appetite* 2017;116:223-31. doi: 10.1016/j.appet.2017.05.002
62. University UN, Organization WH. Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation: . Rome: Food & Agriculture Org. 2004:17-24.
63. Cepeda-Benito A, Gleaves DH, Fernandez MC, et al. The development and validation of Spanish versions of the State and Trait Food Cravings

Questionnaires. *Behav Res Ther* 2000;38(11):1125-38. doi: 10.1016/s0005-7967(99)00141-2

64. Meule A, Lutz A, Vogele C, et al. Food cravings discriminate differentially between successful and unsuccessful dieters and non-dieters. Validation of the Food Cravings Questionnaires in German. *Appetite* 2012;58(1):88-97. doi: 10.1016/j.appet.2011.09.010
65. Fairburn CG, Beglin SJ. Assessment of Eating Disorders - Interview or Self-Report Questionnaire. *Int J Eat Disorder* 1994;16(4):363-70.
66. Hilbert A, Tuschen-Caffier B. Eating Disorder Examination-Questionnaire 2: Deutschsprachige Übersetzung (2. Auflage). Tübingen: dgvt-Verlag. 2016.
67. Meule A, Hermann T, Kuubler A. A short version of the Food Cravings Questionnaire - Trait: the FCQ-T-reduced. *Frontiers in Psychology* 2014;5 doi: ARTN 19010.3389/fpsyg.2014.00190
68. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *J Psychopathol Behav* 2004;26(1):41-54. doi: Doi 10.1023/B:Joba.0000007455.08539.94
69. Ehring T, Svaldi J, Tuschen-Caffier B, et al. Validierung der Difficulties in Emotion Regulation Scale–deutsche Version (DERS-D). University of Münster 2013.
70. *Guideline for Good Clinical Practice (ICH E6 (R2), Step 5.* Retrieved from https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2016.
71. Marcus MD, Kalarchian MA. Binge eating in children and adolescents. *Int J Eat Disorder* 2003;34:S47-S57. doi: 10.1002/eat.10205
72. Tanofsky-Kraff M, Ranzenhofer LM, Yanovski SZ, et al. Psychometric properties of a new questionnaire to assess eating in the absence of hunger in children and adolescents. *Appetite* 2008;51(1):148-55. doi: 10.1016/j.appet.2008.01.001
73. Organization WH. International statistical classification of diseases and related health problems (11th ed.) 2019.

FIGURE LEGEND

Figure 1. Study flow chart from screening (T_0) to 3-month-FU (T_5).

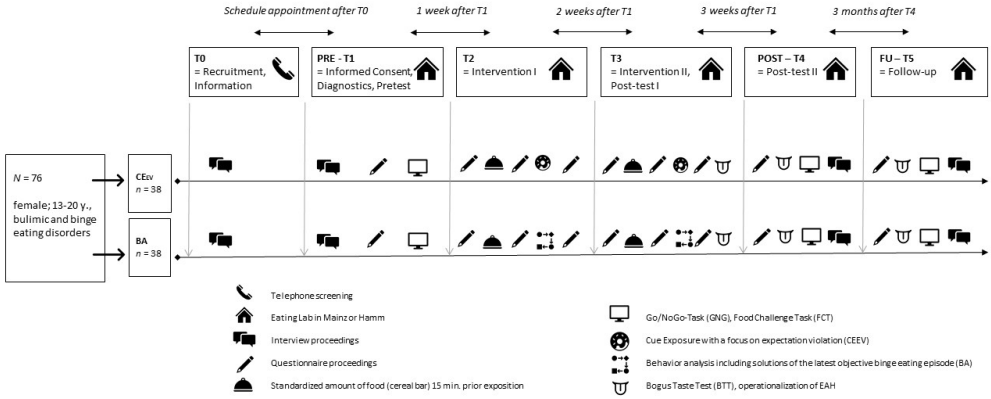

Figure 1. Study flow chart from screening (T0) to 3-month-FU (T5).

338x190mm (96 x 96 DPI)

Supplementary material for the manuscript "Modified Cue Exposure for Adolescents with Binge Eating Behaviour: Study Protocol of a Randomised Pilot Trial called EXI$_{(ea)}$T"

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Translated version of the CE_{EV} standardised session protocol (Session 1)

1. Brief welcome, clarification of questions, thank the participant for completing the questionnaires

2. Participant's most recent food intake, current level of hunger, and current desire to eat are assessed with VAS (0-100)

3. Standardised food intake (cereal bar); 15 minutes before intervention

4. Implementation of CE_{EV}

4.1. Psychoeducation (aims and procedure of the intervention)

"*Exercises with the aim of learning to manage difficulties in food-related situations are often implemented in psychotherapy, because patients perceive them as helpful. In such exercises, a person is confronted with food that typically activates their desire to eat (e.g. chocolate, crisps) and that often leads to problematic behaviour accompanied by the feeling of loss of control (e.g. binge eating). In this exercise, we want to practise this confrontation without the binge eating happening. By doing this exercise, the desire to eat the food can be reduced and you can gain the experience of keeping yourself and your behaviour under control. During the exercise, different aspects of the problematic behaviour can be focused on. We would like to focus on dysfunctional expectations, e.g. "If I see delicious food, I cannot resist eating it." During the exercise, we can explore whether your expectation comes true or not; e.g. that you cannot resist eating it when you see or taste chocolate. If the expectation does not come true (which is very likely) and you realise that you can withstand the urge to eat, the probability of future binge eating can be reduced.*
What happens during the exercise?
During the exercise, you and your therapist look at the food closely and examine it. First, you will smell the food, then you will lick the food and finally you will eat a piece of it without losing control and without binge eating. During the exercise, your therapist will support you and ask you repeatedly about your desire to eat, how difficult it is not to eat the food, and how likely you would be to lose control if your therapist was not present. The exercise can initially be very tiring, but over time your desire to eat and therefore the necessary effort will decrease and your confidence that you will not lose control will increase."

4.2. Identification of dysfunctional expectations

"*To check your expectations in the exercise, it is important to know what your expectations are before starting. Expectations can be very different and sometimes*

you are not consciously aware of them. Together with your therapist, you will identify your overeating expectations. For the exercise, it is helpful to raise your awareness with regard to your dysfunctional expectations in the specific food-related situation."

Examples of possible expectations:

Expectations of the confrontation with your typical binge eating food	"If I see delicious food, I will not be able to resist eating it." "If I am confronted with sweets, I will lose control."
Expectations on the process when first signs of desire to eat appear	"If I realise I have a desire to eat, I will eat." "If I begin to eat, I will never be able to stop."
Expectations on control over craving/desire to eat	"I cannot resist the desire to eat." "I am not able to regulate myself."
Expectations about myself	"After eating I will feel better." "After eating I will feel less of a failure."
Further additions	

➔ Please write down two individual expectations on two index cards!

CAVE: Guide the participant to formulate two dysfunctional expectations as an "If CS-then CR" link. If the participant has difficulties formulating individual expectations, offer the two following standardised expectations:

1. "If there's delicious food in front of me, I will not be able to resist eating it."
2. "If I eat a small piece of delicious food, I will not be able to stop eating more."

4.3. The participant rates her level of hunger, her desire to eat, as well as her expectation of overeating on a VAS (0-100)

4.4. Implementation of CE_{EV}

- The exposure ends as soon as the desire to eat has decreased by 50% compared to the highest rating, but after a maximum of 70 minutes.
- Follow the standardised instructions in the table (see below). The questions should be repeated every five minutes. Meanwhile, the participant rates her desire to eat as well as her expectation of overeating with regard to the exposed food on a VAS (0-100).
- If the desire to eat has not decreased by 50% and there is time left after one round (instructions 1 to 4), repeat these instructions (1 to 4).

Instruction Cue Exposure

First, imagery to establish a connection to the place where binge eating usually occurs:

"*I would like you to imagine the place where binge eating usually occurs. You are invited to close your eyes or to look at a fixed a point in this room to increase your concentration on this exercise. Now imagine that you are in the place where binge eating usually occurs. Where are you sitting (at home in your kitchen or living room)? What do you see? What do you smell? Where are the foods? What are you doing? What are you experiencing in your body? How do you feel? How strong is your desire to eat (scale 0-100)? Where do you feel the desire to eat (i.e. is your mouth starting to water or is your stomach contracting?"*

To increase the transfer to daily life, the following questions should be asked between every instruction and after the cue exposure. In addition, the imagery should be repeated, especially in participants who report a low desire to eat in the session due to the presence of the therapist:

"If you were at home, what would you do? Would your desire to eat be similar? How likely would you be to binge eat at home? What would be different at home?"

1. *Smell the peel and take a piece of it on your hand and also smell the piece.*
   - ➔ *What does the smell do to you, how difficult is it not to eat X? How strong is your desire to eat X at the moment?*
   - ➔ *How does it feel to take X in your hand, how difficult is it not to eat X? How strong is your desire to eat X at the moment?*

2. *Do you think it would be more difficult not to eat X if you were to touch X with your tongue? Or would you lose control? Let`s find out.*
   - ➔ *What`s happening? Why didn`t you lose control?*
   - ➔ *Was it difficult not to eat X after licking it?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

3. *Do you think it would be more difficult not to eat X if you bit a little piece out of X? Or would you lose control? Let`s find out.*
   - ➔ *What`s happening? Why didn`t you lose control?*
   - ➔ *Was it difficult to stop eating after the bite?*
   - ➔ *Was it difficult to stop eating after chewing it?*
   - ➔ *How was it possible that you stopped eating?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

4. *How difficult is it not to eat X when you are seeing it at the moment?*
   - ➔ *Why aren't you losing control?*
   - ➔ *What will you take with you from this exercise?*
   - ➔ *What did you learn from this exercise?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

4.5. Participant rates her level of hunger, her desire to eat and her expectation of overeating on a VAS (0-100)

5. Development of two alternative, helpful expectancies
    - Did the two individual expectancies happen? Which expectancies could be more helpful?
    - The new expectancies should be written on two index cards for the participant so that she can attach the cards to a visible place or carry the cards with her: *"It has proven helpful to attach the cards to a visible place in your room or to carry the cards in your purse so that you always have them present."*

6. Discuss home exercises
    - If possible, the exercise should be repeated at least twice at home.
    - Emphasise the reason for the home exercises: "*Our experience is that it is very helpful to repeat the exercise several times at home so that the transferability to daily life can be increased. Changing a habit takes a lot of practice. Have you ever tried to learn anything new in another situation (i.e. a hobby or language)? How did it go? …"*
    - Validation and anticipation of obstacles and avoidance tendencies, i.e. *"Other adolescents reported concerns that doing the home exercise would lead to binge eating/ strong emotions or would trigger negative emotions. How does it feel for you?"*
    - Consider possible times and conditions together with the participant to increase the motivation to do the exercises (i.e. who buys the food or whether the food should be stored by the parents)
    - For standardisation, the exposed binge food of the session should also be used as the food for exposure in the home exercise.
    - Depending on the course of the preceding exposure, the home exercise can be done with the same or with changed dysfunctional expectations.
    - Show the participant the exercise booklet and hand it to her.
    - Show the protocol sheet and explain it. The participant should bring the protocol sheet to the next session.

7. Remind the participant about the second intervention session (T3) and remind her that she should eat sufficiently, but not within the last two hours before the intervention.

8. Participant discharge

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	1, 3, 9-17, see also DRKS00024009
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	17
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 17
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	7-8
	6b	Explanation for choice of comparators	4
Objectives	7	Specific objectives or hypotheses	8-9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9-10, 11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-12, 10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10-11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	10
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10-11
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	10
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-11, 13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	15
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA

Appendices

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Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Patient and Parent informed consent + Supplement (CE_{EV} standardised session protocol)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Modified Cue Exposure for Adolescents with Binge Eating Behaviour: Study Protocol of a Randomised Pilot Trial called EXI(ea)T

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Primary Subject Heading:	Mental health
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Modified Cue Exposure for Adolescents with Binge Eating Behaviour: Study Protocol of a Randomised Pilot Trial called EXI$_{(ea)}$T.

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Word count: 5047

Running Head: MODIFIED CUE EXPOSURE FOR ADOLESCENTS WITH BINGE EATING BEHAVIOUR

Abstract

Introduction: Binge eating (BE) behaviour is highly prevalent in adolescents, and can result in serious metabolic derangements and overweight in the long term. Weakened functioning of the behavioural inhibition system is one potential pathway leading to BE. Food cue exposure focusing on expectancy violation (CE_{EV}) is a short intervention for BE that has proven effective in adults but has never been tested in adolescents. Thus, the current randomised pilot trial evaluates the feasibility of CE_{EV} for adolescents and its efficacy in reducing eating in the absence of hunger (EAH) of binge food items.

Methods and analysis: The trial will include *N* = 76 female adolescents aged between 13 and 20 years with a diagnosis of bulimia nervosa (BN), binge eating disorder (BED), or their subthreshold forms based on the DSM-5. Participants will be randomly assigned to two sessions of CE_{EV} or behavioural analysis (BA), a classical CBT-based intervention. The primary endpoint is the change in EAH measured according to ad libitum consumption of personally preferred binge food in a bogus taste test at post-test based on the intention-to-treat (ITT) population. Key secondary endpoints are changes in EAH of standardised binge food at post-test, in EAH at 3-month follow-up (FU), and in food craving after induction of food cue reactivity at posttest and FU. To identify further valid outcome parameters, we will assess effects of CE_{EV} compared to BA on global ED psychopathology, BE frequency within the last 28 days, body weight, response inhibition, and emotion regulation abilities. Treatment groups will be compared using analysis of covariance (ANCOVA) with intervention as fixed factor and BMI at baseline as covariate.

Ethics and dissemination: This clinical trial has been approved by the Ethics Review Committee of the Medical Association of Rhineland-Palatinate and the Medical Faculty of the Ruhr-University Bochum. The collected data will be disseminated locally and internationally through publications in relevant peer-reviewed journals and will be presented at scientific and clinical conferences. Participants data will only be published in anonymised form.

Strengths and limitations of this study

- $EXI_{(ea)}T$ is a randomised pilot trial comparing cue exposure with expectancy violation (CE_{EV}) to behavioural analysis (BA) of binge eating (BE) episodes, the gold standard intervention of cognitive behaviour therapy (CBT).
- CE_{EV} is informed by previous evidence in adults with BE episodes and youth with obesity integrating age-appropriate material for a transdiagnostic adolescent sample.
- The multimodal assessment approach uses an objective measure as the primary outcome, ad libitum food intake.
- As a multicentre trial, $EXI_{(ea)}T$ enables a generalisation of the proof-of-concept, and contributes to quality assurance in the cooperating centres.
- Due to the short follow-up period of three months, no conclusions about the long-term efficacy of CE_{EV} for eating disorder psychopathology and body weight can be drawn.

Protocol version 9.0, 25/07/2022

Trial registration: German Clinical Trials Register, DRKS00024009, 22/01/2021

INTRODUCTION

Binge eating in adolescents

Binge eating (BE) behaviour refers to recurrent episodes of impulsive overeating accompanied by the feeling of loss of control over eating. About 18% of 16-year-old adolescents reported BE as a single symptom at least sometimes, 8.5% even weekly during the last year.[1 2] BE is a core feature of both bulimia nervosa (BN) and binge eating disorder (BED), which show high prevalences of 0.9% to 3% (BN) and 1.3% to 5% (BED) in youth with overweight.[3 4 5] However, the majority of affected youth do not seek treatment as they associate BE with shame and guilt, leading to a long illness duration (8 to 14 years) and to a persistence of adverse outcomes into adulthood.[5 6]

Available first-line treatments for BE-related disorders in youth are mostly based on "enhanced" cognitive behaviour therapy for EDs (CBT-E).[7] Behavioural analysis (BA) of BE episodes is among the gold standard interventions within CBT-E, and focuses on early symptom changes.[8] CBT-E has been shown to be effective in achieving BE abstinence in almost 50% of patients with BN, but remission rates are lower in youth than in adults, e.g. 29% remitted.[9] Initial findings for CBT-E in adolescents with BED suggest that abstinence rates are comparable to those in adults, ranging between 43 and 61%.[10 11] Given the higher number of early responders in CBT-E compared to other therapy approaches, BA can be seen as at least partially responsible for the rapid therapeutic effects.[12 13]

In sum, at least 50% of youth continue to have BE episodes or certain impulsive eating behaviour patterns as residual symptoms at the end of treatment. One reason for this might be that the direct underlying mechanism - food-related inhibitory control deficits - is rarely targeted in conventional treatment programs.

Inhibitory control as an underlying mechanism

Recent studies emphasize an association of BE with self-reported impulsivity and behaviourally measured inhibitory control deficits.[14 15] Inhibitory control is conceptualised as the ability to inhibit impulsive responses in order to select a more value-based functional behaviour, e.g. eating out of deliberate pleasure instead of impulsivity.[16] Response inhibition in general, and towards food stimuli might be impaired in adults with bulimic-type EDs[17], although evidence for adolescents with BE is predominantly only available for non-clinical samples.[18 19] Moreover, a recent study

revealed that adolescents with obesity and BED displayed a poorer inhibition performance compared to normal-weight adolescents[20], although the study did not allow for any conclusions on stimulus specificity. Studies examining samples with overweight have yielded contradictory findings: While one study reported that children were less effective in food-specific response inhibition[21], we found that adolescent psychiatric inpatients showed a rather generally impaired inhibitory control irrespective of ED pathology.[22] Analogous to adults, it can be assumed that there is a specific subgroup of youth with impulsive eating patterns and inhibitory control deficits, presumably more generalised based on their current stage of development.

In this framework, the dual-pathway model by Hofmann and colleagues[23] postulates that BE is controlled via two processes - 1. automatic, unconscious processes and 2. reflexive, conscious processes. Automatic responses to food stimuli are primarily associated with the rewarding component of impulsive behaviour. This appetitive responding may be related to reward sensitivity and food-related inhibition deficits and is based on a heightened reactivity to palatable food cues or non-food cues that signal the availability of tempting food, i.e. food cue-reactivity.[24 25] In turn, top-down processes primarily involve executive functions such as emotion regulation and general inhibition abilities and are designed to counteract automatic behaviour.[26 27] A weakened reflexive system can be overridden by strong impulsive reactions to appetitive food stimuli, resulting in food craving and BE. Crucially, the impaired inhibitory control seems to be met with a hyperresponsive reward system due to neuroadaptive changes in reward circuits (see maintenance model for BE).[28]

In line with the dual-process model, recent findings have highlighted the interaction between emotion regulation and inhibitory control in terms of predicting BE.[29 30] In an adult sample with self-reported ED symptoms, eating expectancies mediated the relationship between emotion regulation difficulties and BE, but only in individuals with reward-based inhibition deficits.[30] Moreover, adolescents with poor self-reported inhibition experienced more uncontrolled eating, but only in the case of a negative mood.[31]

In sum, food-related inhibitory control deficits might act as an underlying perpetuating mechanism of BE, but studies examining interventions to address these deficits are lacking. So far, research has not identified an intervention for impulsive eating

behaviour that integrates food stimuli and has proven to be superior to other approaches.[10 32]

Inhibitory learning approach to exposure

One option to improve food-related inhibitory control is food cue exposure (CE), i.e. exposure to typical binge food and its stimulus characteristics, such as the taste or smell of a food, while preventing food consumption. The effect of CE on BE is often measured by the intake of palatable foods in laboratory paradigms, i.e. eating in the absence of hunger (EAH) in line with Birch and colleagues.[33]

Researchers have discussed two potential working mechanisms for CE in the area of BE: habituation and inhibitory learning. Initially, CE was seen as classical extinction training derived from principles of learning theory. Treatment manuals postulating habituation as a rationale recommend that patients focus on their desire to eat on a psychological and physiological level, while food stimuli (conditioned stimuli, CS) are presented in order to reduce food cue reactivity (conditioned appetitive responses, CR) via in-session habituation.[34] Since the 1980s, CE with habituation has mainly been researched for the treatment of BN, although over the years, this intervention was forgotten somewhat due to the complexity of implementing it in clinical practice.[35-38]

Recently, CE has been experiencing a revival in the treatment of BN and BED, with inhibitory control being used as rationale.[39-41] Research in anxiety disorders suggests that repeated exposure creates a new inhibitory association such that binge food then also signals the non-availability of the unconditioned eating response, i.e. a new CS-noUS pairing.[42] To enhance inhibitory learning in CE, sessions should be designed so as to maximize the discrepancy between the expectancy of overeating and what really happens, namely no overeating.[43] Magson and colleagues[44] even assume that habituation occurs because of inhibitory learning - if patients are exposed to food in such a way that their CS-US expectancies are not violated, no habituation processes will occur and they will be vulnerable to relapses. This assumption is also in line with observations that habituation within and between sessions, i.e. desire to eat, is not beneficially related to EAH and weight loss[39 43 45], whereas changes in expectancies were found to mediate treatment success regarding EAH.[43] Accordingly, CE should optimize the violation of idiographic beliefs about eating behaviour when confronted with the relevant binge food (e.g. “If I have milk chocolate next to me when I am sitting

alone doing my homework, I have to eat the whole bar."). In CE with expectancy violation (CE_{EV}), these beliefs are checked against what actually happens, i.e. the feared BE does not occur, which may strengthen the inhibitory pathway (e.g. "If I have milk chocolate […], I am able to resist eating the whole bar."). Moreover, there is evidence that different impulsive response domains (affective, cognitive and behavioural) exist and improvements in one domain in turn favour inhibition control in the other two domains.[46] It can be assumed that there is an improvement in self-efficacy through the implementation of positive expectations, such as being able to resist binge foods (cognitive self-control) and, with a delay, also an improvement in affective and behavioral self-control. Consequently, possible underlying mechanisms of change such as emotion regulation abilities and inhibitory control will be altered due to their interactions with BE expectancies.[29-31]

Food cue exposure with expectancy violation influencing BE

A recent review[44] included 16 studies that investigated CE in adults with BE, three of which focused on expectancy violation.[39 43 45] Regardless of its focus, CE significantly reduced overeating expectancies, desire to eat, and EAH as measured by kcal consumption during a subsequent bogus taste test (BTT).[39] In addition, relative to a lifestyle intervention, CE_{EV} was more effective in reducing the number of BE episodes and also in reducing weight from baseline to 3-month follow-up (FU) in women with overweight (d = 0.67 and d = 0.65).[43] Moreover, EAH for exposed food decreased significantly in CE_{EV} (d = 0.35 – 0.81)[45], but this finding did not generalize to non-exposed food.[43] The opposite findings emerged for non-personalised exposed food items.[43 45] It can be suggested that personalised food items might better capture individual learning processes and should thus be included in CE in order to achieve more profound changes in food-related inhibitory control.

With regard to mechanisms of change, both generic and idiographic BE expectancies were found to be more effectively disconfirmed in $CE_{EV,}$ with d = 4.12 and d = 9.50, compared to active control interventions.[43 45] Moreover, in a recent within-group pilot study, significant improvements in expectancies about ability to tolerate distress were found after five sessions of CE_{EV} in women with BED.[47] Interestingly, expectancy violations (idiographic CS-US and distress tolerance expectancies) were found prior to changes in BE frequency, emphasizing their assumed potential for subsequent

habituation processes.[44 47] To date, only one study has assessed self-reported impulsivity: Participants were randomized to an 8-session group intervention focusing on CE or a control intervention with both conditions including self-monitoring techniques.[40] No between-group differences emerged. To the best of our knowledge, however, no research has assessed the efficacy of CE for food-related inhibitory control and emotion regulation.

With respect to adolescent samples, CE has only been applied in two studies to date.[39 48] In patients with BN aged 14 to 19 years who had not responded well to CBT, a 12-session CE with habituation was effective in significantly decreasing BE and purging from baseline to post-treatment and at 6-month FU.[48] Schyns and colleagues[39] compared CE_{EV} with a lifestyle intervention in a clinical sample of adolescents with obesity. The main focus of the lifestyle intervention was on providing psychoeducation to increase healthier eating and physical activity. Two sessions of CE_{EV} were conducted and EAH was assessed as the primary endpoint, operationalised by the percentage of consumed kcal in a BTT relative to the personal daily energy requirement. CE_{EV} significantly reduced the ad libitum food intake of an exposed food item (chocolate mousse) and of non-exposed food items compared to the control condition (d = 0.80 and d = 0.76). Contrary to findings in adults, the exposure effects generalised to further highly palatable food, suggesting that adolescents might learn faster.[39] It can therefore be assumed that not all relevant food cues need to be integrated into CE_{EV} sessions. However, adherence to homework exercises was poor, suggesting the need for stronger guidance of CE_{EV} at home, especially in this young age group.

To sum up, evidence in adults and in adolescents with obesity indicates medium to large effect sizes regarding the improvement of EAH via ad libitum food intake, eating psychopathology, and weight reduction after only two sessions of CE_{EV}. However, more RCTs are needed to support this inhibitory learning approach to exposure in adolescents with BE.

STUDY AIMS AND HYPOTHESES

The current pilot study, called $EXI_{(ea)}T$, targets the feasibility and efficacy of CE_{EV} for adolescents with recurrent BE episodes relative to BA in a multicentre randomised trial. $EXI_{(ea)}T$ is an acronym for *EXIT* strategies as a way out of binge *ea*ting. The diagnosis

of BE episodes in adolescents can be challenging for a number of reasons. First, adolescents who still live at home and are financially dependent of their parents do not have unrestricted access to food - therefore the consumption during a BE and the frequency can be externally limited. Second, there is evidence that loss of control over eating may be more important, especially in view of the large amounts of food that can be eaten due to pubertal developmental spurts. Accordingly, it is important to consider also subthreshold BN and BED in adolescents. Marcus and Kalarchian[49] next to Tanofsky-Kraff and colleagues[50] have proposed modified criteria for BED in childhood and adolescence. For the diagnosis "recurrent episodes of BE persisting over a period of 3 months" are required which has also found its way into the new ICD-11 criteria. Based on our clinical ED expertise, we applied a low-threshold cut-off of only three objective BE episodes within the last three months although a typical clinical picture is present. Recurrent BE episodes are therefore operationalised by a diagnosis of BN, BED, or Other Specified Feeding or Eating Disorder (OSFED-BN/BED). Taken together, the aims of $EXI_{(ea)}T$ are to investigate (1) the application of CE_{EV} compared to BA in a transdiagnostic adolescent sample with BE, (2) whether CE_{EV} effectively reduces EAH and food craving at post-treatment and at 3-month FU, and (3) the effect of CE_{EV} on global ED pathology, number of binge episodes and weight, and (4) on underlying mechanisms of change, i.e. expectancy violations. We hypothesize that CE_{EV} will be superior to BA in reducing ad libitum food intake of personally preferred exposed and non-exposed binge foods beyond physiological needs at post-test. With regard to secondary endpoints, we expect CE_{EV} to lead to a stronger decrease in ad libitum intake of standardised binge food, food craving, ED psychopathology, and BE frequency and to a stronger weight reduction at FU compared to BA. Moreover, we hypothesize that adolescents in the CE_{EV} condition will additionally benefit with respect to larger violations of BE expectancies. On an exploratory level, we will analyse potential moderating effects of food-related response inhibition and emotion regulation abilities.

METHODS AND ANALYSIS

Patient and Public Involvement

The modified CE was developed from clinical work with adolescents with EDs. To ensure appropriateness of CE_{EV} for the relevant clinical group and age range, a

preliminary study on treatment expectations was conducted with a student sample aged 18-25 years who experienced stress-induced chocolate cravings. Help-seeking rates in adolescents that meet BN or BED criteria are very low with 11.6% and 22.3%[51] what underlines the significant delay from onset of symptoms to accessing eating disorder-specific treatment.[52] Consequently, for economic and ethical reasons, we included young students in the preliminary study. The results on treatment expectations were used to optimise the CE before inclusion of the first patient.

Study design

This study is a randomized (with a 4:4 allocation ratio), controlled, double-blind multicentre trial comparing CE_{EV} to BA. Recruitment, data collection, interventions and data analysis are conducted in two departments of child and adolescent psychiatry and psychotherapy at the University Hospital Bochum and the University Medical Center Mainz.

Participants and recruitment

The following inclusion criteria are applied 1) female adolescents aged 13;00 to 20;11 years; 2) presence of recurrent BE episodes (at least three objective episodes within the last three months with loss of control and clinically significant distress/functional impairment) assessed via an expert interview (Eating Disorder Examination, EDE[53 54]); 3) diagnosis of BN, BED or OSFED-BN/BED (BN or BED of low frequency and/or limited duration) based on DSM-5; 4) sufficient knowledge of the German language; and 5) written informed consent of the participant and the caregivers. Adolescents are excluded if they show 1) severe psychopathological comorbidities (such as severe depressive episodes, borderline personality disorder, substance use disorder, dissociative disorders, diagnosis of non-suicidal self-injury based on DSM-5), although mild to moderate comorbidities do not lead to exclusion as long as ED symptoms are the core symptoms; 2) anorexia nervosa; 3) immediate need for inpatient treatment due to acute suicidality or BE/purging at a high frequency; and 4) ongoing outpatient treatment with a focus on ED-specific interventions (e.g. CE, mirror exposure). The participants are recruited via press releases, flyers, and social media, as well as in schools, and youth centres in Hamm and Mainz and the surrounding areas. In addition,

cooperations with counselling centres, child and adolescent psychiatrists and psychotherapists, and pediatricians are used for recruitment.

Study flow and procedure

The study flow is illustrated in Fig. 1. First, subjects and their caregivers are informed about the aims and procedure of the study in a telephone interview (T_0). In addition, the inclusion and exclusion criteria are checked.

Please insert Figure 1 here.

At the beginning of each session, participants` most recent food intake is assessed and their current levels of hunger and desire to eat are measured on a 100mm visual analogue scale (VAS). At the baseline assessment (T_1), participants undertake two computer-based tasks (Food Challenge Task, FCT[55]; Go/NoGo Task, GNG[56 57]), before their weight, height and body fat percentage are measured by bioelectrical impedance analysis (BIA). Moreover, general psychopathology is assessed and the EDE-II and an interview on binge food (in which participants are asked to state four personally preferred binge foods) are conducted. After a short break, relevant parts of the Diagnostic Interview for Mental Disorders in Children and Adolescents (Kinder-DIPS-OA)[58] are conducted. The remaining self-rating questionnaires are completed online via REDCap.[59] The randomisation takes place after T_1 using a blockwise procedure (block sizes of four) by Sealed Envelope that run automatically in the REDCap data management. To ensure that assessors (experienced and trained psychologists) are blinded, the study leaders randomize the participants. Two sessions of CE_{EV} or BA follow at T_2 and T_3. Participants are requested to eat sufficiently prior to the appointments but not within the last two hours before the intervention. To avoid hunger during the interventions, participants are asked to eat a cereal bar 15 minutes before the intervention. After CE_{EV} and BA, current levels of hunger, desire to eat, and the two relevant overeating expectancies in the CE_{EV} group are assessed again. At the end of the intervention sessions, participants are strongly encouraged to repeat the exercise at home to increase the transferability to daily life. We look for specific favourable times of day for the implementation and anticipate possible difficulties or obstacles. The participants also receive an exercise booklet with general information

about the intervention as well as detailed instruction and protocol sheets. At the beginning of T_3, these home exercises, obstacles to implementation and potential solutions are discussed and participants are again encouraged to continue with the exercises at home. At the end of T_3, a BTT with all four preferred binge foods is conducted. The BTT is a valid and sensitive instrument to investigate whether experimental manipulations effect food intake with respect to EAH[60] and has been applied in obese adolescents.[39] To ensure that participants were not aware of the aims of the experimental hypotheses, they are asked to evaluate the taste of the foods on a rating sheet during a set time period of 15 min.[60] They are invited to eat as much as they need to evaluate the taste. Before and after the rating, the weight of the food is measured out of sight of the participants and the consumed calories are calculated. The dependent variable is the percentage of consumed calories in relation to the individual's daily energy demand with respect to age and gender (recommendation of the World Health Communication).

At the post-assessment (T_4), the frequency of home exercises is discussed again. Next, a BTT is performed with standardised non-exposed food items (milkshakes), and the computer-based tasks are repeated. Binge-purge behaviours are assessed. The questionnaires can be completed at home. The post-assessment is repeated at T_5 (FU) three months after T_4. At T_5, the BTT is conducted with three preferred and one standardised binge foods. Any outstanding questionnaires are completed on site to avoid missing data. At the end of T5, participants receive an allowance of 50€.

Interventions

Both conditions include two face-to-face sessions with a maximum duration of 70 minutes each. Following a standardised session protocol (see Supplement), the interventions are delivered by experienced CBT therapists at each site. In the CE_{EV} group, participants are exposed to two out of four personally preferred binge food items. Two individual overeating expectancies are used during exposure, and if a subject has difficulties in formulating expectancies, standardised overeating expectances are applied (i.e. "If I see delicious food, I won't be able to resist eating it."). Directly before CE_{EV} and every five minutes, subjects are asked to rate their current levels of hunger, desire to eat the exposed food, and the two relevant overeating expectancies on a 100mm VAS. The exposure ends as soon as the desire to eat has decreased by 50%

compared to the highest rating, but at the latest after 70 minutes. After the exposure, two alternative, helpful expectancies are developed together with the therapist and are written on two index cards so that the participant can carry them with her. Control group participants undergo a BA of the last BE episode based on the SORKC model.[61] First, situational and preceding factors as well as the cognitive, emotional, physiological and behavioural reactions of the participant are identified. In addition, consequences of the behaviour are detected. The BA ends with a solution analysis by identifying effective skills to prevent BE, but also after 70 minutes at the latest.

Diagnostic and outcome assessments

Patient characteristics and diagnostics

Besides sociodemographic information such as age and school type, general information such as ongoing therapy, and previous treatments is gathered. In addition, information to compute the socioeconomic status (SES; Winkler-Index[62]) is obtained. To identify possible comorbidities, the Freiburger Screening for Mental Disorders (FSP)[63] is used as screening instrument. The sections on depressive disorders, anxiety disorders, ADHD, conduct disorders, tic disorders, enuresis, encopresis and non-suicidal self-injury disorder are administered routinely in the Kinder-DIPS-OA; the other sections are explored in the case of relevant answers in the previously administered FSP. Eating disorder psychopathology is assessed with the well-established interview EDE which allows an accurate clinical judgment of global ED psychopathology over the last 28 days and is considered the gold standard for ED-specific diagnostics.[53 54] Other diagnostics are general psychopathology[58], last food intake, level of hunger and desire to eat. Instruments and their psychometric characteristics are illustrated in Table 1.

Table 1. Assessment plan from screening (T_0) to 3-month follow-up (T_5).

Variable	Instrument	Description	Score indication	Assessment moments				
				T_1	T_2	T_3	T_4	T_5
Diagnostics								
Eligibility screen		Inclusion and exclusion criteria		X				
Clinical baseline data		e.g. age, school type, treatments		X				
General psychopathology - self-report	Strengths and Difficulties Questionnaire (SDQ)[64 65]	25 items range from 0-40	Higher scores indicate more externalising and internalising problems	X				
Psychological impairment	Freiburger Screening für psychische Störungen (FSP)[63]	Screening questions for 14 mental disorders with 29 items		X				
General psychopathology - clinical judgment	Diagnostic Interview for Mental Disorders in Children and Adolescents (Kinder-DIPS-OA)[58]	Screening for mental disorders according to the DSM-IV-TR[66] and ICD-10[67]		X				
Eating disorder psychopathology - clinical judgment	Eating Disorder Examination (EDE)[53 54]	Semi-structured interview with 22 and four subscales “Restraint”, “Eating concerns”, Shape concerns”, and “Weight concerns”	Higher scores indicate more eating disorder psychopathology	X				
Primary outcome								
Eating in the absence of hunger (EAH)	Bogus Taste task (BTT, preferred food items)[60]	Exposition to their personally preferred food items	Higher consumed calories indicate more EAH			X		X
Secondary outcomes								
Eating in the absence of hunger (EAH)	Bogus Taste task (BTT, standardised food items)[60]	Exposition to milkshakes	Higher consumed calories indicate more EAH				X	X
Momentary food craving	Food Challenge Task (FCT)[55]	Craving is measured with the Food Craving Questionnaire-	Higher scores indicate higher intensity of craving	X			X	X

		State (FCQ-S)[68], consists of 15 items range from 15-75				
Binge eating	Eating Disorder Examination (EDE)[53 54]			X	X	X
Eating disorder psychopathology - self-report	Eating Disorder Examination-Questionnaire (EDE-Q)[69 70]	Self-report questionnaire with 22 items	Higher scores indicate more eating disorder psychopathology	X	X	X
Weight, height, body fat	Bioelectrical impedance analysis (BIA), InBody770*			X	X	X
Food craving	Food Craving Questionnaire-Trait (FCQ-T-r)[71]	15 items range from 15-90	Higher scores indicate higher frequency and intensity of food craving	X	X	X
Moderator variables						
Response inhibition	Go/NoGo Task (GNG Task)[56 57]	Affective shifting task with high-caloric vs. neutral food stimuli; 16 blocks with a total of 320 trials	Higher number of commission errors indicate lower inhibition skills	X	X	X
Emotion regulation	Difficulties in Emotion Regulation Scale (DERS) [72 73]	36 items range from 36-180	Higher scores indicate more difficulties in emotion regulation	X	X	X
Treatment expectation and evaluation						
Treatment expectation	Expectation of Improvement and Suitability of Treatment Form (EIST)[74]	Two items, rated on a 10-point Likert scale	Higher scores indicate positive treatment expectation	X	X	X
Treatment evaluation	Patient Questionnaire on Therapy Expectation and Evaluation (PATHEV)[75]	11 items, rated on a 5-point Likert scale	Higher score indicate better treatment evaluation	X	X	X

Notes. T_0 = Telephone interview; T_1 = Baseline assessment; T_2 = Intervention session 1; T_3 = Intervention session 2; T_4 = Post-assessment; T_5 = Follow-up; * Body fat is only measured at the Mainz site.

Primary Outcome

EAH is assessed with BTT, a valid and sensitive instrument to investigate whether experimental manipulations affect food intake.[60] Participants are exposed to their personally preferred binge foods and are asked to evaluate the taste of the food on a rating sheet. They are invited to eat as much as they need to evaluate the taste. Before and after the rating, the weight of the food is measured and the consumed calories are calculated. The dependent variable is the percentage of consumed calories in relation to the individual's daily energy requirements with respect to age and gender in line with the recommendations of the United Nations University and the World Health Organization.[76]

Secondary Outcomes

EAH is measured with standardized food items in the BTT. Momentary food craving is assessed with the FCT in which a five-minute video with tasty foods is presented to induce craving.[55] After participants have watched the video, the experience of craving is measured with the Food Craving Questionnaire-State (FCQ-S).[68] The FCT has proven to be valid for the standardised induction of food cue reactivity to measure momentary food craving.[55] Other secondary outcome measures are binge eating, eating disorder psychopathology[69 70], weight, height, body fat and trait food craving (FCQ-T-r).[71]

Moderators

To identify possible moderating effects, emotion regulation is measured with the Difficulties in Emotion Regulation Scale (DERS)[72 73], and response inhibition is assessed with a modified personalised GNG affective shifting task (high-calorie food category vs. neutral category).[56 57] Neutral stimuli (flower, towel) and high-calorie foods (chocolate, pizza) are presented as Go or NoGo stimuli (depending on the block). To determine participants` personal taste preferences, prior to the GNG Task, they are asked to rate 30 high-calorie food stimuli on a 7-point Likert scale (0 = not at all palatable to 6 = extremely palatable). The ten personally most palatable food stimuli are then used in the task. Participants are instructed to press a button when watching a relevant stimulus ("Go") and to not press the button when watching an irrelevant stimulus ("NoGo"). The task consists of 16 blocks with 50% of the stimuli presented as Go stimuli and 50% as NoGo stimuli in each block. Participants receive instructions at

the beginning of each block. Each stimulus is presented for 500ms with an inter-trial interval of 1000ms. Dependent variables are participants` reaction times and number of commission errors (false reactions to a NoGo instruction) and omission errors (missing reactions to a Go instruction). The GNG task is a widely used task to measure response inhibition.[22]

Additional assessments

Adherence control

Attrition rate and study dropouts are assessed in both treatment groups. Manual adherence across the different therapists is achieved through standardised treatment protocols, online trainings and fortnightly supervisions by a licensed expert in ED treatment (TL) across both participating centres.

Treatment Expectation and Evaluation

Treatment expectation and evaluation are assessed with the Expectation of Improvement and Suitability of Treatment Form (EIST)[74] and the Patient Questionnaire on Therapy Expectation and Evaluation (PATHEV)[75].

Sample size calculation

The sample size calculation is based on the publication of Schyns and colleagues[39], which reports an effect size of d = 0.8 between groups for the percentage of consumed kcal during the taste test relative to the daily energy requirements (experimental group: mean 57% (N = 21; SD = 68%), control group: mean 146% (N = 19; SD = 141%)). When calculating the pooled standard deviation (SD_{pooled} = 118.5%) and assuming an effect size of 0.8, this results in an absolute difference of 75% in the mean between groups, which can be considered as relevant. When assuming a two-sided significance level, a power of 90%, an effect size of d = 0.8 and a sample size of 68 patients (=2x34 patients) will be needed to detect a significant treatment difference at post-assessment when using a t-test. As the duration of treatment is very short (two weeks only), we assume that patient loss due to non-compliance will be minimal. To account for 10% dropouts[39], 76 patients should be randomised. The calculation was performed using SAS Version 9.4.

Data analysis plan

Regarding the primary outcome EAH, treatment groups will be compared using an analysis of covariance (ANCOVA) with intervention as fixed factor and BMI at baseline as covariate. The primary analysis is performed on the ITT population consisting of all patients randomised next to per-protocol (PP) analyses. The secondary parameters are mostly continuous parameters, and will be analysed using AN(C)OVAs and t-tests. Sample characteristics will be provided. A p-value of $< .05$ is considered as statistically significant (two-sided). Missing values will not be replaced, however an analysis of potential missing data patterns will be presented. There will be several sensitivity analyses, e.g. by considering additional covariates.

Data availability

The research data generated during this study will be available on reasonable request by the corresponding authors. Anonymised data use by other researchers not involved in the study may be done with prior agreement.

ETHICS AND DISSEMINATION

Ethics and safety aspects

The trial will be conducted according to the principles of ICH-GCP and appropriate legal regulations, and will adhere to the Declaration of Helsinki in its latest version. Participating individuals are provided with treatment as usual (TAU which consists of BA) for EDs according to good clinical practice.[77] The study protocol including amendments has been and will be approved by the responsible ethics committees. Important protocol modifications will be reported to the German Clinical Trials Register and to the journal. Participants and caregivers must provide written informed consent before beginning the study. CE is generally well tolerated[39 43], and risks for participants are not known or expected. Trained clinical staff will be available to monitor safety concerns and support patients during/after treatment.

Dissemination plan

The collected data will be disseminated locally and internationally through publications in relevant peer-reviewed journals and will be presented at scientific and clinical conferences. Participants data will only be published in anonymised form.

DISCUSSION

Research on effective treatment elements for BE in adolescents is still limited, leaving a gap in knowledge on interventions that might enhance outcomes for this age group. One promising way to achieve this might be to target food-related inhibitory control as an underlying perpetuating mechanism of BE. Recent results suggest a successful adaptation of CE_{EV} for pathological eating behavior. However, little is known about the feasibility and efficacy of CE_{EV} for adolescents with recurrent BE episodes. Thus, the findings of $EXI_{(ea)}T$ might clarify whether CE_{EV} is accepted by a transdiagnostic adolescent sample and whether it is able to reduce the ad libitum consumption of highly palatable foods when satiated as well as ED pathology. Furthermore, we will elucidate the role of CS-US expectancy violations, response inhibition, and emotion regulation in $CE_{EV.}$ The strengths of $EXI_{(ea)}T$ lie in the inclusion of a credible, active control condition, considered as the gold standard intervention of CBT-E to treat BE, and the use of an objective measure to assess changes, i.e. ad libitum food intake, as the primary efficacy endpoint. Moreover, the CE_{EV} treatment protocol includes the most relevant CE strategies to maximize treatment success[44], i.e. in-vivo exposure, personally preferred food cues and non-food cues (due to imagery of trigger situations at the beginning of session), occasionally eating allowed and personal CS-US expectancies identified. Additionally, to overcome poor homework adherence, we offer a detailed exercise booklet, discuss implementation problems and debrief all exercises at the beginning of session 2. On the level of limitations, it should be noted that $EXI_{(ea)}T$ cannot evaluate the efficacy of CE_{EV} as an add-on intervention to CBT-E as a whole. BA is a very strong control intervention, which could make it difficult to identify a significant superiority of $CE_{EV.}$ Moreover, we did not ask explicitly for “new” expectations that might arise during the CE_{EV}. Similarly, it should be pointed out that there is no data monitoring committee to review accumulating data, which may affect the independence of the analyses. In addition, our decision to use the DSM-5 criteria and not the age-adapted criteria for BED[49 78] or modified ICD-11 criteria for bulimic

disorders[79], which emphasize the subjective loss of control (LOC), needs to be explored with respect to recruitment procedures. Indeed, we have not found prior evidence that CE_{EV} is also a valuable intervention with respect to LOC eating. However, if CE_{EV} is effective and feasible for adolescents with BE, we might conduct a confirmatory randomised trial in order to test CE_{EV} as a useful adjunct to first-line treatment.

Trial status

Recruitment for this trial started in April 2021 and is ongoing.

Contributions

All authors contributed to the design and conception of this study. HP, IK, JE and TL elaborated the study protocol and gained ethical approval. HP and IK drafted the manuscript and JE, SL, JP, LD, FH and TL revised the manuscript critically. All authors have read and approved the final version of the article submitted.

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Competing interests

TL receives royalties for textbooks in the field of eating disorders from Hogrefe, Kohlhammer, Springer and DeGruyter as well as funding from the German Ministry of Education and Research (BMBF) for studies in the field of eating disorders and obesity. HP receives royalties for a therapy manual for BE from Hogrefe. The other authors declare that they have no competing interests.

Ethics approval

Ethical approval has been granted by the Ethics Review Committee of the Medical Association of Rhineland-Palatinate (No. 2020-14980) and of the Medical Faculty of the Ruhr-University Bochum (No. 20-7051 BR).

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES

1. Olsen EM, Koch SV, Skovgaard AM, et al. Self-reported symptoms of binge-eating disorder among adolescents in a community-based Danish cohort-A study of prevalence, correlates, and impact. *Int J Eat Disord* 2021;54(4):492-505. doi: 10.1002/eat.23458 [published Online First: 20201231]
2. Flament MF, Henderson K, Buchholz A, et al. Weight Status and DSM-5 Diagnoses of Eating Disorders in Adolescents From the Community. *J Am Acad Child Adolesc Psychiatry* 2015;54(5):403-11 e2. doi: 10.1016/j.jaac.2015.01.020 [published Online First: 20150216]
3. Campbell K, Peebles R. Eating disorders in children and adolescents: state of the art review. *Pediatrics* 2014;134(3):582-92. doi: 10.1542/peds.2014-0194
4. Kjeldbjerg ML, Clausen L. Prevalence of binge-eating disorder among children and adolescents: a systematic review and meta-analysis. *Eur Child Adolesc Psychiatry* 2021 doi: 10.1007/s00787-021-01850-2 [published Online First: 20210727]
5. Marzilli E, Cerniglia L, Cimino S. A narrative review of binge eating disorder in adolescence: prevalence, impact, and psychological treatment strategies. *Adolesc Health Med Ther* 2018;9:17-30. doi: 10.2147/AHMT.S148050 [published Online First: 20180105]
6. Goldschmidt AB, Wall MM, Loth KA, et al. The course of binge eating from adolescence to young adulthood. *Health Psychol* 2014;33(5):457-60. doi: 10.1037/a0033508 [published Online First: 20130826]
7. Mulkens S, Waller G. New developments in cognitive-behavioural therapy for eating disorders (CBT-ED). *Curr Opin Psychiatry* 2021;34(6):576-83. doi: 10.1097/YCO.0000000000000745 [published Online First: 2021/08/31]
8. Fairburn CG. Cognitive behaviour therapy and eating disorders: Guilford Press 2008.
9. Gorrell S, Matheson BE, Lock J, et al. Remission in adolescents with bulimia nervosa: Empirical evaluation of current conceptual models. *Eur Eat Disord Rev* 2020;28(4):445-53. doi: 10.1002/erv.2729 [published Online First: 20200304]
10. Hilbert A, Petroff D, Neuhaus P, et al. Cognitive-Behavioral Therapy for Adolescents with an Age-Adapted Diagnosis of Binge-Eating Disorder: A Randomized Clinical Trial. *Psychother Psychosom* 2020;89(1):51-53. doi: 10.1159/000503116 [published Online First: 20190918]
11. Hilbert A, Petroff D, Herpertz S, et al. Meta-analysis on the long-term effectiveness of psychological and medical treatments for binge-eating disorder. *Int J Eat Disord* 2020;53(9):1353-76. doi: 10.1002/eat.23297 [published Online First: 20200625]
12. Linardon J, Brennan L, de la Piedad Garcia X. Rapid response to eating disorder treatment: A systematic review and meta-analysis. *Int J Eat Disord* 2016;49(10):905-19. doi: 10.1002/eat.22595 [published Online First: 2016/08/17]
13. Fairburn CG, Bailey-Straebler S, Basden S, et al. A transdiagnostic comparison of enhanced cognitive behaviour therapy (CBT-E) and interpersonal psychotherapy in the treatment of eating disorders. *Behav Res Ther* 2015;70:64-71. doi: 10.1016/j.brat.2015.04.010 [published Online First: 2015/05/23]

14. Giel KE, Teufel M, Junne F, et al. Food-Related Impulsivity in Obesity and Binge Eating Disorder-A Systematic Update of the Evidence. *Nutrients* 2017;9(11) doi: 10.3390/nu9111170 [published Online First: 20171027]
15. Schag K, Schonleber J, Teufel M, et al. Food-related impulsivity in obesity and binge eating disorder - a systematic review. *Obes Rev* 2013;14(6):477-95. doi: 10.1111/obr.12017 [published Online First: 20130121]
16. Verbruggen F, Logan GD. Automatic and controlled response inhibition: associative learning in the go/no-go and stop-signal paradigms. *J Exp Psychol Gen* 2008;137(4):649-72. doi: 10.1037/a0013170
17. Wu MD, Hartmann M, Skunde M, et al. Inhibitory Control in Bulimic-Type Eating Disorders: A Systematic Review and Meta-Analysis. *Plos One* 2013;8(12) doi: ARTN e8341210.1371/journal.pone.0083412
18. Ames SL, Kisbu-Sakarya Y, Reynolds KD, et al. Inhibitory control effects in adolescent binge eating and consumption of sugar-sweetened beverages and snacks. *Appetite* 2014;81:180-92. doi: 10.1016/j.appet.2014.06.013 [published Online First: 20140617]
19. Byrne ME, Shank LM, Altman DR, et al. Inhibitory control and negative affect in relation to food intake among youth. *Appetite* 2021;156:104858. doi: 10.1016/j.appet.2020.104858 [published Online First: 20200904]
20. Kittel R, Schmidt R, Hilbert A. Executive functions in adolescents with binge-eating disorder and obesity. *Int J Eat Disorder* 2017;50(8):933-41. doi: 10.1002/eat.22714
21. Nederkoorn C, Coelho JS, Guerrieri R, et al. Specificity of the failure to inhibit responses in overweight children. *Appetite* 2012;59(2):409-13. doi: 10.1016/j.appet.2012.05.028 [published Online First: 2012/06/06]
22. Deux N, Schlarb AA, Martin F, et al. Overweight in adolescent, psychiatric inpatients: A problem of general or food-specific impulsivity? *Appetite* 2017;112:157-66. doi: 10.1016/j.appet.2017.01.031
23. Hofmann W, Friese M, Strack F. Impulse and Self-Control From a Dual-Systems Perspective. *Perspect Psychol Sci* 2009;4(2):162-76. doi: 10.1111/j.1745-6924.2009.01116.x [published Online First: 2009/03/01]
24. Jansen A, Schyns G, Bongers P, et al. From lab to clinic: Extinction of cued cravings to reduce overeating. *Physiol Behav* 2016;162:174-80. doi: 10.1016/j.physbeh.2016.03.018 [published Online First: 2016/03/21]
25. van den Akker K, Stewart K, Antoniou EE, et al. Food Cue Reactivity, Obesity, and Impulsivity: Are They Associated? *Current Addiction Reports* 2014;1(4):301-08. doi: 10.1007/s40429-014-0038-3
26. Legenbauer T, Preuss H. Improving Impulse and Emotion Regulation in Binge Eating Disorder: Possible Application and First Results of the ImpulsE Manual. *Kindh Entwickl* 2019;28(4):210-19. doi: 10.1026/0942-5403/a000292
27. Preuss H, Leister L, Pinnow M, et al. Inhibitory control pathway to disinhibited eating: A matter of perspective? *Appetite* 2019;141:104297. doi: 10.1016/j.appet.2019.05.028 [published Online First: 20190522]
28. Treasure J, Leslie M, Chami R, et al. Are trans diagnostic models of eating disorders fit for purpose? A consideration of the evidence for food addiction. *Eur Eat Disord Rev* 2018;26(2):83-91. doi: 10.1002/erv.2578 [published Online First: 2018/01/18]
29. Van Malderen E, Goossens L, Verbeken S, et al. The interplay between self-regulation and affectivity in binge eating among adolescents. *Eur Child Adolesc*

Psychiatry 2019;28(11):1447-60. doi: 10.1007/s00787-019-01306-8 [published Online First: 20190309]

30. Smith KE, Mason TB, Peterson CB, et al. Relationships between eating disorder-specific and transdiagnostic risk factors for binge eating: An integrative moderated mediation model of emotion regulation, anticipatory reward, and expectancy. *Eat Behav* 2018;31:131-36. doi: 10.1016/j.eatbeh.2018.10.001 [published Online First: 2018/10/26]
31. Van Malderen E, Kemps E, Verbeken S, et al. Food for mood: Experimentally induced negative affect triggers loss of control over eating in adolescents with low inhibitory control. *Int J Eat Disord* 2021;54(3):388-98. doi: 10.1002/eat.23422 [published Online First: 20201204]
32. Ince B, Schlatter J, Max S, et al. Can we change binge eating behaviour by interventions addressing food-related impulsivity? A systematic review. *J Eat Disord* 2021;9(1):38. doi: 10.1186/s40337-021-00384-x [published Online First: 2021/03/20]
33. Birch LL, Fisher JO, Davison KK. Learning to overeat: maternal use of restrictive feeding practices promotes girls' eating in the absence of hunger. *Am J Clin Nutr* 2003;78(2):215-20. doi: 10.1093/ajcn/78.2.215 [published Online First: 2003/07/30]
34. Jansen A, Van den Hout MA, De Loof C, et al. A case of bulimia successfully treated by cue exposure. *J Behav Ther Exp Psychiatry* 1989;20(4):327-32. doi: 10.1016/0005-7916(89)90064-5
35. Fairburn C. A cognitive behavioural approach to the treatment of bulimia. *Psychol Med* 1981;11(4):707-11. doi: 10.1017/s0033291700041209
36. Leitenberg H, Gross J, Peterson J, et al. Analysis of an Anxiety Model and the Process of Change during Exposure Plus Response Prevention Treatment of Bulimia Nervosa. *Behav Ther* 1984;15(1):3-20. doi: 10.1016/S0005-7894(84)80038-6
37. Jansen A, Broekmate J, Heymans M. Cue-exposure vs self-control in the treatment of binge eating: a pilot study. *Behav Res Ther* 1992;30(3):235-41. doi: 10.1016/0005-7967(92)90069-s [published Online First: 1992/05/01]
38. Rosen JC, Leitenberg H. Bulimia nervosa: Treatment with exposure and response prevention. *Behav Ther* 1982;13(1):117-24. doi: https://doi.org/10.1016/S0005-7894(82)80055-5
39. Schyns G, Roefs A, Smulders FTY, et al. Cue exposure therapy reduces overeating of exposed and non-exposed foods in obese adolescents. *J Behav Ther Exp Psychiatry* 2018;58:68-77. doi: 10.1016/j.jbtep.2017.09.002 [published Online First: 2017/09/13]
40. Schag K, Rennhak SK, Leehr EJ, et al. IMPULS: Impulsivity-Focused Group Intervention to Reduce Binge Eating Episodes in Patients with Binge Eating Disorder - A Randomised Controlled Trial. *Psychother Psychosom* 2019;88(3):141-53. doi: 10.1159/000499696 [published Online First: 2019/05/21]
41. Ferrer-Garcia M, Pla-Sanjuanelo J, Dakanalis A, et al. Eating behavior style predicts craving and anxiety experienced in food-related virtual environments by patients with eating disorders and healthy controls. *Appetite* 2017;117:284-93. doi: 10.1016/j.appet.2017.07.007
42. Craske MG, Treanor M, Conway CC, et al. Maximizing exposure therapy: An inhibitory learning approach. *Behaviour Research and Therapy* 2014;58:10-23. doi: 10.1016/j.brat.2014.04.006

43. Schyns G, van den Akker K, Roefs A, et al. Exposure therapy vs lifestyle intervention to reduce food cue reactivity and binge eating in obesity: A pilot study. *J Behav Ther Exp Psychiatry* 2020;67:101453. doi: 10.1016/j.jbtep.2019.01.005 [published Online First: 2019/02/09]
44. Magson NR, Handford CM, Norberg MM. The Empirical Status of Cue Exposure and Response Prevention Treatment for Binge Eating: A Systematic Review. *Behav Ther* 2021;52(2):442-54. doi: 10.1016/j.beth.2020.06.005 [published Online First: 2021/02/25]
45. Schyns G, Roefs A, Mulkens S, et al. Expectancy violation, reduction of food cue reactivity and less eating in the absence of hunger after one food cue exposure session for overweight and obese women. *Behav Res Ther* 2016;76:57-64. doi: 10.1016/j.brat.2015.11.007 [published Online First: 2015/12/10]
46. Berkman ET, Graham AM, Fisher PA. Training Self-Control: A Domain-General Translational Neuroscience Approach. *Child Dev Perspect* 2012;6(4):374-84. doi: 10.1111/j.1750-8606.2012.00248.x
47. Norberg MM, Handford CM, Magson NR, et al. Reevaluating Cue Exposure and Response Prevention in a Pilot Study: An Updated Treatment for Binge Eating Disorder. *Behav Ther* 2021;52(1):195-207. doi: 10.1016/j.beth.2020.04.003 [published Online First: 2021/01/24]
48. Martinez-Mallen E, Castro-Fornieles J, Lazaro L, et al. Cue exposure in the treatment of resistant adolescent bulimia nervosa. *Int J Eat Disord* 2007;40(7):596-601. doi: 10.1002/eat.20423 [published Online First: 2007/07/04]
49. Marcus MD, Kalarchian MA. Binge eating in children and adolescents. *Int J Eat Disorder* 2003;34:S47-S57. doi: 10.1002/eat.10205
50. Tanofsky-Kraff M, Marcus MD, Yanovski SZ, et al. Loss of control eating disorder in children age 12 years and younger: proposed research criteria. *Eat Behav* 2008;9(3):360-5. doi: 10.1016/j.eatbeh.2008.03.002 [published Online First: 20080407]
51. Forrest LN, Smith AR, Swanson SA. Characteristics of seeking treatment among U.S. adolescents with eating disorders. *Int J Eat Disord* 2017;50(7):826-33. doi: 10.1002/eat.22702 [published Online First: 20170321]
52. Hamilton A, Mitchison D, Basten C, et al. Understanding treatment delay: Perceived barriers preventing treatment-seeking for eating disorders. *Aust N Z J Psychiatry* 2022;56(3):248-59. doi: 10.1177/00048674211020102 [published Online First: 20210712]
53. Fairburn CG, Cooper Z. The Eating Disorder Examination (12th edition). In: Fairburn CG, Wilson GT, eds. 12th edition ed: Guilford Press 1993:317–60
54. Hilbert A, Tuschen-Caffier B. Eating Disorder Examination (German version, 2nd ed.): dgvt-Verlag 2016.
55. Van den Eynde F, Claudino AM, Mogg A, et al. Repetitive transcranial magnetic stimulation reduces cue-induced food craving in bulimic disorders. *Biol Psychiatry* 2010;67(8):793-5. doi: 10.1016/j.biopsych.2009.11.023 [published Online First: 2010/01/12]
56. Meule A, Lutz A, Krawietz V, et al. Food-cue affected motor response inhibition and self-reported dieting success: a pictorial affective shifting task. *Frontiers in Psychology* 2014;5 doi: 10.3389/fpsyg.2014.00216
57. Meule A, Kubler A. Double trouble. Trait food craving and impulsivity interactively predict food-cue affected behavioral inhibition. *Appetite* 2014;79:174-82. doi: 10.1016/j.appet.2014.04.014 [published Online First: 20140423]

58. Margraf J, Cwik JC, Pflug V, et al. Structured clinical interviews for mental disorders across the lifespan: Psychometric quality and further developments of the DIPS Open Access interviews.[Strukturierte klinische Interviews zur Erfassung psychischer Störungen über die Lebensspanne: Gütekriterien und Weiterentwicklungen der DIPS-Verfahren.] *Z Kl Psych Psychoth* 2017;46:176-86.
59. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208 [published Online First: 2019/05/13]
60. Robinson E, Haynes A, Hardman CA, et al. The bogus taste test: Validity as a measure of laboratory food intake. *Appetite* 2017;116:223-31. doi: 10.1016/j.appet.2017.05.002 [published Online First: 20170502]
61. Kanfer FH, Philips JS. Lerntheoretische Grundlagen der Verhaltenstherapie. München: Kindler 1970.
62. Winkler J, Stolzenberg H. Adjustierung des Sozialen-Schicht-Index für die Anwendung im Kinder- und Jugendgesundheitssurvey (KiGGS). Wismarer Diskussionspapiere. Wismar: Hochschule Wismar, Fakultät für Wirtschaftswissenschaften, 2009.
63. Hölzel, Ower, Berger, et al. FSP - Freiburger Screening für Psychische Störungen nach ICD-10 [in preparation]. Kurzzeitbehandlung bei psychischen Störungen in der Hausarztpraxis: Elsevier-Verlag.
64. Goodman R, Meltzer H, Bailey V. The Strengths and Difficulties Questionnaire: a pilot study on the validity of the self-report version. *Eur Child Adolesc Psychiatry* 1998;7(3):125-30. doi: 10.1007/s007870050057 [published Online First: 1998/11/24]
65. Lohbeck A, Schultheiss J, Petermann F, et al. The German Self-Report Version of the Strengths and Difficulties Questionnaire (SDQ-Deu-S): Psychometric Properties, Factor Structure, and Critical Values. *Diagnostica* 2015;61(4):222-35. doi: 10.1026/0012-1924/a000153
66. American Psychiatric Association APA. Diagnostic and Statistical Manual of Mental Disorders, Text Revision. DSM-IV-TR. Washington DC: APA 2000.
67. World Health Organisation. International statistical classification of diseases and related health problems (10th ed.)2016.
68. Meule A, Lutz A, Vögele C, et al. Food cravings discriminate differentially between successful and unsuccessful dieters and non-dieters. Validation of the Food Cravings Questionnaires in German. *Appetite* 2012;58(1):88-97. doi: https://doi.org/10.1016/j.appet.2011.09.010
69. Fairburn CG, Beglin SJ. Assessment of Eating Disorders - Interview or Self-Report Questionnaire. *Int J Eat Disorder* 1994;16(4):363-70.
70. Hilbert A, Tuschen-Caffier B. Eating Disorder Examination-Questionnaire (German version, 2nd ed.): dgvt-Verlag 2016.
71. Meule A, Hermann T, Kuubler A. A short version of the Food Cravings Questionnaire - Trait: the FCQ-T-reduced. *Frontiers in Psychology* 2014;5 doi: ARTN 19010.3389/fpsyg.2014.00190
72. Gutzweiler R. Validity and Reliability of the German Version of the DERS in a Clinical and a School Sample of Adolescents. *Z Klin Psychol Psychother* 2018;47(4) 274-86.
73. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the

difficulties in emotion regulation scale. *J Psychopathol Behav* 2004;26(1):41-54. doi: Doi 10.1023/B:Joba.0000007455.08539.94

74. Agras WS, Crow SJ, Halmi KA, et al. Outcome predictors for the cognitive behavior treatment of bulimia nervosa: Data from a multisite study. *Am J Psychiat* 2000;157(8):1302-08. doi: DOI 10.1176/appi.ajp.157.8.1302
75. Schulte D. Patient questionnaire on therapy expectation and evaluation (PATHEV). *Z Kl Psych Psychoth* 2005;34(3):176-87. doi: 10.1026/1616-3443.34.3.176
76. United Nations University UN, World Health Organization. Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation: Rome: Food & Agriculture Org. 2004:17-24.
77. *Guideline for Good Clinical Practice (ICH E6 (R2), Step 5.* Retrieved from https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2016.
78. Tanofsky-Kraff M, Ranzenhofer LM, Yanovski SZ, et al. Psychometric properties of a new questionnaire to assess eating in the absence of hunger in children and adolescents. *Appetite* 2008;51(1):148-55. doi: 10.1016/j.appet.2008.01.001 [published Online First: 20080207]
79. World Health Organization. International statistical classification of diseases and related health problems (11th ed.)2019.

FIGURE LEGEND

Figure 1. Study flow chart from screening (T_0) to 3-month-FU (T_5).

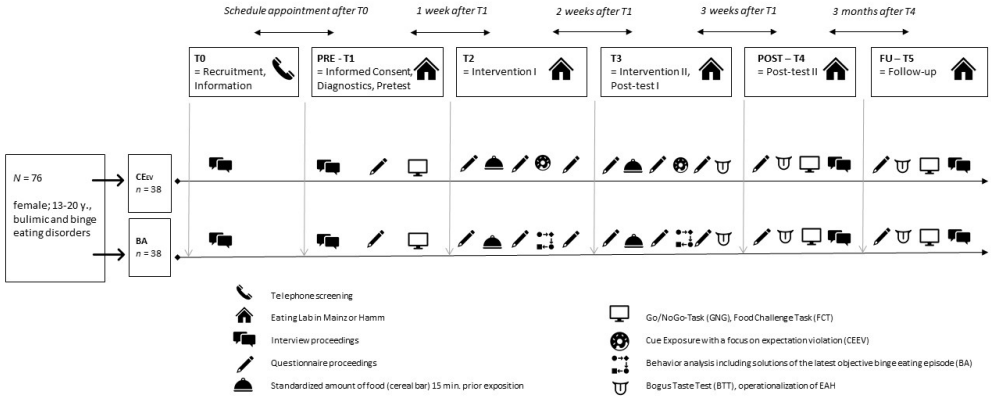

Figure 1. Study flow chart from screening (T0) to 3-month-FU (T5).

338x190mm (96 x 96 DPI)

Supplementary material for the manuscript "Modified Cue Exposure for Adolescents with Binge Eating Behaviour: Study Protocol of a Randomised Pilot Trial called EXI$_{(ea)}$T"

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Translated version of the CE_{EV} standardised session protocol (Session 1)

1. Brief welcome, clarification of questions, thank the participant for completing the questionnaires

2. Participant's most recent food intake, current level of hunger, and current desire to eat are assessed with VAS (0-100)

3. Standardised food intake (cereal bar); 15 minutes before intervention

4. Implementation of CE_{EV}

4.1. Psychoeducation (aims and procedure of the intervention)

"*Exercises with the aim of learning to manage difficulties in food-related situations are often implemented in psychotherapy, because patients perceive them as helpful. In such exercises, a person is confronted with food that typically activates their desire to eat (e.g. chocolate, crisps) and that often leads to problematic behaviour accompanied by the feeling of loss of control (e.g. binge eating). In this exercise, we want to practise this confrontation without the binge eating happening. By doing this exercise, the desire to eat the food can be reduced and you can gain the experience of keeping yourself and your behaviour under control. During the exercise, different aspects of the problematic behaviour can be focused on. We would like to focus on dysfunctional expectations, e.g. "If I see delicious food, I cannot resist eating it." During the exercise, we can explore whether your expectation comes true or not; e.g. that you cannot resist eating it when you see or taste chocolate. If the expectation does not come true (which is very likely) and you realise that you can withstand the urge to eat, the probability of future binge eating can be reduced.*
What happens during the exercise?
During the exercise, you and your therapist look at the food closely and examine it. First, you will smell the food, then you will lick the food and finally you will eat a piece of it without losing control and without binge eating. During the exercise, your therapist will support you and ask you repeatedly about your desire to eat, how difficult it is not to eat the food, and how likely you would be to lose control if your therapist was not present. The exercise can initially be very tiring, but over time your desire to eat and therefore the necessary effort will decrease and your confidence that you will not lose control will increase."

4.2. Identification of dysfunctional expectations

"*To check your expectations in the exercise, it is important to know what your expectations are before starting. Expectations can be very different and sometimes*

you are not consciously aware of them. Together with your therapist, you will identify your overeating expectations. For the exercise, it is helpful to raise your awareness with regard to your dysfunctional expectations in the specific food-related situation."

Examples of possible expectations:

Expectations of the confrontation with your typical binge eating food	"If I see delicious food, I will not be able to resist eating it." "If I am confronted with sweets, I will lose control."
Expectations on the process when first signs of desire to eat appear	"If I realise I have a desire to eat, I will eat." "If I begin to eat, I will never be able to stop."
Expectations on control over craving/desire to eat	"I cannot resist the desire to eat." "I am not able to regulate myself."
Expectations about myself	"After eating I will feel better." "After eating I will feel less of a failure."
Further additions	

➔ Please write down two individual expectations on two index cards!

CAVE: Guide the participant to formulate two dysfunctional expectations as an "If CS-then CR" link. If the participant has difficulties formulating individual expectations, offer the two following standardised expectations:

1. "If there's delicious food in front of me, I will not be able to resist eating it."
2. "If I eat a small piece of delicious food, I will not be able to stop eating more."

4.3. The participant rates her level of hunger, her desire to eat, as well as her expectation of overeating on a VAS (0-100)

4.4. Implementation of CE_{EV}

- The exposure ends as soon as the desire to eat has decreased by 50% compared to the highest rating, but after a maximum of 70 minutes.
- Follow the standardised instructions in the table (see below). The questions should be repeated every five minutes. Meanwhile, the participant rates her desire to eat as well as her expectation of overeating with regard to the exposed food on a VAS (0-100).
- If the desire to eat has not decreased by 50% and there is time left after one round (instructions 1 to 4), repeat these instructions (1 to 4).

Instruction Cue Exposure

First, imagery to establish a connection to the place where binge eating usually occurs:

"*I would like you to imagine the place where binge eating usually occurs. You are invited to close your eyes or to look at a fixed a point in this room to increase your concentration on this exercise. Now imagine that you are in the place where binge eating usually occurs. Where are you sitting (at home in your kitchen or living room)? What do you see? What do you smell? Where are the foods? What are you doing? What are you experiencing in your body? How do you feel? How strong is your desire to eat (scale 0-100)? Where do you feel the desire to eat (i.e. is your mouth starting to water or is your stomach contracting?"*

To increase the transfer to daily life, the following questions should be asked between every instruction and after the cue exposure. In addition, the imagery should be repeated, especially in participants who report a low desire to eat in the session due to the presence of the therapist:

"If you were at home, what would you do? Would your desire to eat be similar? How likely would you be to binge eat at home? What would be different at home?"

1. *Smell the peel and take a piece of it on your hand and also smell the piece.*
   - ➔ *What does the smell do to you, how difficult is it not to eat X? How strong is your desire to eat X at the moment?*
   - ➔ *How does it feel to take X in your hand, how difficult is it not to eat X? How strong is your desire to eat X at the moment?*

2. *Do you think it would be more difficult not to eat X if you were to touch X with your tongue? Or would you lose control? Let`s find out.*
   - ➔ *What`s happening? Why didn`t you lose control?*
   - ➔ *Was it difficult not to eat X after licking it?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

3. *Do you think it would be more difficult not to eat X if you bit a little piece out of X? Or would you lose control? Let`s find out.*
   - ➔ *What`s happening? Why didn`t you lose control?*
   - ➔ *Was it difficult to stop eating after the bite?*
   - ➔ *Was it difficult to stop eating after chewing it?*
   - ➔ *How was it possible that you stopped eating?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

4. *How difficult is it not to eat X when you are seeing it at the moment?*
   - ➔ *Why aren't you losing control?*
   - ➔ *What will you take with you from this exercise?*
   - ➔ *What did you learn from this exercise?*
   - ➔ *How difficult is it not to eat X at the moment? How strong is your desire to eat X at the moment?*

4.5. Participant rates her level of hunger, her desire to eat and her expectation of overeating on a VAS (0-100)

5. Development of two alternative, helpful expectancies
    - Did the two individual expectancies happen? Which expectancies could be more helpful?
    - The new expectancies should be written on two index cards for the participant so that she can attach the cards to a visible place or carry the cards with her: *"It has proven helpful to attach the cards to a visible place in your room or to carry the cards in your purse so that you always have them present."*

6. Discuss home exercises
    - If possible, the exercise should be repeated at least twice at home.
    - Emphasise the reason for the home exercises: "*Our experience is that it is very helpful to repeat the exercise several times at home so that the transferability to daily life can be increased. Changing a habit takes a lot of practice. Have you ever tried to learn anything new in another situation (i.e. a hobby or language)? How did it go? …"*
    - Validation and anticipation of obstacles and avoidance tendencies, i.e. *"Other adolescents reported concerns that doing the home exercise would lead to binge eating/ strong emotions or would trigger negative emotions. How does it feel for you?"*
    - Consider possible times and conditions together with the participant to increase the motivation to do the exercises (i.e. who buys the food or whether the food should be stored by the parents)
    - For standardisation, the exposed binge food of the session should also be used as the food for exposure in the home exercise.
    - Depending on the course of the preceding exposure, the home exercise can be done with the same or with changed dysfunctional expectations.
    - Show the participant the exercise booklet and hand it to her.
    - Show the protocol sheet and explain it. The participant should bring the protocol sheet to the next session.

7. Remind the participant about the second intervention session (T3) and remind her that she should eat sufficiently, but not within the last two hours before the intervention.

8. Participant discharge

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	1, 3, 9-17, see also DRKS00024009
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	17
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 17
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	7-8
	6b	Explanation for choice of comparators	4
Objectives	7	Specific objectives or hypotheses	8-9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9-10, 11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-12, 10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10-11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	10
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10-11
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	10
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-11, 13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	15
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Patient and Parent informed consent + Supplement (CE_{EV} standardised session protocol)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.