Early Change Trajectories in Cognitive-Behavioral Therapy for Binge-Eating Disorder

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Abstract

Rapid response is considered the most well-established outcome predictor across treatments of binge-eating disorder (BED), including cognitive-behavioral therapy (CBT). This study sought to identify latent trajectories of early change in CBT and compare them to common rapid response classifications. In a multicenter randomized trial, 86 adults with BED (DSM-IV) or subsyndromal BED provided weekly self-reports of binge eating over the first four weeks of CBT, which were analyzed to predict binge eating, depression, and body mass index at posttreatment, 6-, and 18-month follow-up. Using latent growth mixture modeling, three patterns of early change - including moderate and low decreasing - as well as low stable binge eating were identified, which significantly predicted binge-eating remission at 6-month follow-up. Other classifications of rapid response based on Receiver Operating Characteristics curve analyses or on the literature (≥ 10% reduction in binge eating at week 1, ≥ 70% reduction in binge eating at week 4) only predicted posttreatment remission or overall depression, respectively. Latent change trajectories, but not other rapid response classifications, predicted binge-eating frequency over time. A fine-grained analysis of change over the first four weeks of CBT for BED revealed different trajectories of early change in binge eating that led to an improved prediction of binge-eating outcome, compared to that of common rapid response classifications. Thorough monitoring of early change trajectories during treatment may have clinical utility.

Keywords: binge-eating disorder; eating disorder; psychotherapeutic processes; cognitive behavior therapy; prediction

Early Change Trajectories in Cognitive-Behavioral Therapy for Binge-Eating Disorder

Binge-eating disorder (BED), characterized by recurrent binge eating in the absence of regular compensatory behaviors, is associated with increased eating disorder and general psychopathology, comorbid mental disorders such as depression, overweight and obesity, and impaired quality of life (American Psychiatric Association [APA], 2013*)*. For individuals with BED, cognitive-behavioral therapy (CBT) is considered the most well-established specialty treatment (Association of the Scientific Medical Societies [AWMF], 2011), leading to large and long-lasting improvements of binge-eating and associated psychopathology (Hilbert et al., 2012; Vocks et al., 2010). Given its efficacy provoking remission from binge eating in about 50% of patients (Brownley et al., 2016; Grilo, 2017; Hay, 2013; Iacovino, Gredysa, Altman, & Wilfley, 2012; Wilson, 2011), one important question is how to identify patients with non-response as early as possible in order to tailor the treatment to their needs and improve their outcome.

While pretreatment predictors of outcome in BED have not consistently been identified (Vall & Wade, 2015), research on the prognostic significance of patterns of change during treatment revealed that rapid response, typically defined as a 65-70% reduction in binge eating over the first four weeks of treatment, is a positive prognostic indicator of remission from binge eating across various specialist treatment approaches for BED, including CBT (Grilo, Masheb, & Wilson, 2006; Grilo, White, Wilson, Gueorguieva, & Masheb, 2012; Hilbert, Hildebrandt, Agras, Wilfley, & Wilson, 2015; Safer & Joyce, 2011; Zunker et al., 2010), with predictive effects extending up to 18 months following treatment cessation in two studies (Hilbert et al., 2015; Safer & Joyce, 2011), but not in another study (Grilo et al., 2012). However, the predictive effect of rapid response on binge eating outcome in BED was found to be small, and inconsistent effects were documented for related outcomes such as depression and weight loss (for a review

see Linardon, Brennan, & de la Piedad Garcia, 2016). In addition, in several studies, Receiver Operating Characteristics (ROC) curve analyses, as used by Grilo et al. (2006, 2012), led to other definitions of rapid response with lower sensitivity and specificity for predicting remission from binge eating (Hilbert et al., 2015; Safer & Joyce, 2011; Zunker et al., 2010), with this non-replication limiting the generalization of the predictive value of rapid response (for a review see Nazar et al., 2016).

Studies from other areas of mental health using latent growth mixture modeling (LGMM), a method for identifying and comparing latent classes of change patterns (Muthén & Muthén, 2000), have suggested that early changes during therapy are more complex than those reflected in simple rapid versus non-rapid response patterns (e.g., Lutz et al., 2014; Lutz, Stulz, & Köck, 2009; Stulz, Lutz, Leach, Lucock, & Barkham, 2007). For example, patients with depression and panic disorder in CBT (Lutz et al., 2009, 2014) revealed early latent trajectories of rapid response: moderate, slow, or no improvement, and rapid deterioration at varying symptom levels. These change patterns differentially predicted treatment outcome at posttreatment (Lutz et al., 2009, 2014) and follow-up (Lutz et al., 2014), with rapid response predicting greatest improvement and other patterns predicting lower improvements. LGMM-identified change patterns were reported to add to the prediction of treatment outcome through early response patterns (Rubel et al., 2015).

This study sought to examine latent classes of early change in binge eating regarding binge-eating symptomatology, depression, and body mass index (BMI, kg/m^2) outcomes within a randomized clinical study of CBT for full and subsyndromal BED (de Zwaan et al., 2017). It was hypothesized that the LGMM-identified classification would significantly predict eating disorder outcomes, but not related outcomes of depression and BMI, at posttreatment and follow-up;

would differ from "conventionally determined" rapid response versus non-rapid response (cf. Grilo et al., 2012); and would exceed the predictive value of conventionally determined rapid versus non-rapid response.

Method

Individuals with full and subsyndromal BED ($N = 178$) were recruited through advertising and clinic referrals at seven treatment sites in Germany and Switzerland for a randomized comparison of individual CBT and Internet-based guided self-help, based on CBT principles ($N = 89$ per condition; INTERBED study). Methodological detail is given elsewhere (de Zwaan et al., 2012, 2017). Ethical approval was granted by site-specific Institutional Review Boards. The study was registered at Current Controlled Trials (ISRCTN40484777) and at the German Clinical Trials Register (DRKS00000409). For this study, only data for the CBT arm were used ($N = 89$), as the required session-wise assessments of binge eating were available in the CBT arm only.

After a telephone screening, eligible participants were invited to a diagnostic visit during which informed consent was obtained, and clinical interviews and self-report questionnaires were used in order to ascertain inclusion. Inclusion criteria were: age $\geq$ 18 years, 27.0 kg/m^2 $\leq$ body mass index (BMI) $\leq$ 40.0 kg/m^2, calculated from measured height and weight, and DSM-IV-TR criteria for BED or subsyndromal BED (de Zwaan et al., 2012, 2017) as ascertained by the semi-structured eating disorder interview Eating Disorder Examination (EDE; Fairburn & Cooper, 1993; Hilbert & Tuschen-Caffier, 2016a) with established reliability and validity (Berg, Peterson, Frazier, & Crow, 2012). Subsyndromal BED allowed for inclusion of patients who lacked one of the DSM-IV-TR criteria (a frequency of less than 2 days with objective binge-eating episodes in 6 months, no marked distress, or the presence of only 2 instead of 3 of the 5

behavioral indicators; de Zwaan et al., 2012, 2017) and was present in 14.0% of CBT patients, while the remainder presented with full-syndrome BED. A total of 94.0% of the patients fulfilled the DSM-5 criteria of BED (APA, 2013). Further, sufficient German language skills and private access to the Internet were required. Patients were allowed to take psychotropic medication (except for antipsychotics or other weight-affecting drugs) and were asked not to modify medications during the trial. Exclusion criteria were: any major medical condition that would interfere with treatment (e.g., type 1 diabetes mellitus, thyroid problems), pregnancy or lactation, ongoing psychotherapy, current bulimia nervosa, current substance abuse, psychosis including schizophrenia and bipolar I disorder, or current significant suicidal ideation.

Treatment

CBT, based on the manual by Hilbert and Tuschen-Caffier (2010), offered 20, 50-min individual sessions with a therapist over four months. CBT was comprised of (1) an initial treatment phase for motivational enhancement; (2) an intensive treatment phase with modules on eating behavior, body image, and stress; and (3) a self-management phase for relapse prevention. Patients were offered CBT twice weekly for month 1, once weekly for month 2 to month 3, and bi-weekly for month 4. The treatment was delivered by master's level clinical psychologists or residents in psychosomatic medicine who received training and were regularly supervised. Therapist adherence across CBT sessions was excellent (Brauhardt et al., 2014).

Assessments

For determining change in binge eating, the number (counts) of objective binge-eating episodes (OBEs) over the past seven days, defined as consumption of an unusually large amount of food accompanied by a subjective experience of loss of control over eating (APA, 2013), was assessed before each treatment session using the binge-eating item of the Eating Disorder

Examination-Questionnaire (EDE-Q; Fairburn & Beglin, 1994; Hilbert & Tuschen-Caffier, 2016b), the validated self-report version of the EDE (Berg et al., 2012), applied to the previous seven days. In the assessment of the number of binge-eating episodes, the EDE-Q converges with the EDE and self-monitoring (Grilo, Masheb, & Wilson, 2001a, b). Because two CBT sessions were held per week in month 1, the second session was selected for determining early change trajectories of binge eating, resulting in one EDE-Q-based self-report assessment of binge eating for each of the first four weeks of treatment.

Outcome assessments were conducted at pretreatment, posttreatment (after four months of treatment), and at 6- and 18-month follow-up. At all these timepoints, the EDE was administered to determine binge-eating remission, operationalized as full abstinence from OBEs (i.e., zero OBEs) over the past 28 days (Fairburn & Cooper, 1993; Hilbert & Tuschen-Caffier, 2016a). The following secondary outcomes were examined: binge-eating frequency (i.e., the number of OBEs) over the past 28 days as determined through the EDE; depression severity, measured through the Beck Depression Inventory (BDI-II; 21 items; sum score, 0 to 63, higher scores indicate greater severity) with established reliability and validity (Beck, Steer, & Brown, 1996; Hautzinger, Keller, & Kühner, 2006); and BMI, calculated from measured weight and height (kg/m^2).

Data Analytic Plan

Three different approaches were used to classify early response to treatment. First, latent growth mixture modeling (LGMM; Muthén & Khoo, 1998; Muthén & Muthén, 2000) was used to identify early trajectories of binge eating over the first four weeks of treatment. Using the Mplus 7.11 software (Muthén & Muthén, 1998–2012), the LGMM models on the number (counts) of binge-eating episodes over the past seven days included an intercept, linear, and

quadratic components. The optimal number of classes was determined using the Bayesian information criterion (*BIC*), the adjusted *BIC* (*aBIC*), and the consistent Akaike information criterion (*cAIC*), with the lowest values indicative of the best model fit. The Akaike information criterion (*AIC*) and the log likelihood were also calculated. A total of 200 random starts were used to avoid problems associated with local maxima. Missing data for LGMM analysis (pretreatment: 0.0%; week 1: 7.0%; week 2: 17.4%; week 3: 26.7%; week 4: 14.0%) were handled using maximum likelihood. For sensitivity analysis, the results from the LGMM analysis were compared with those based on multiple imputation, for which parameter estimates and standard errors were averaged across five imputed data sets. The results from this sensitivity analysis were reported only in case of differences in classification of early change trajectories, based on maximum likelihood when compared to those based on multiple imputation.

Second, according to Grilo et al. (2006), receiver operator characteristic (ROC) curves on the number (counts) of binge-eating episodes over the past seven days of each of the first four weeks of treatment regarding posttreatment binge-eating remission were calculated in order to determine rapid response. Weekly area under the curve (*AUC*) was determined as a measure of effect size. Participants with missing posttreatment assessments were considered to be nonremitted. Participants were classified as rapid responders if they experienced reductions in the number of binge-eating episodes that were equal to or greater than the optimal cutoff based upon ROC analyses that best balanced sensitivity and specificity. Third, Grilo et al.'s empirically derived definition (2012) of rapid response as a reduction in the number of binge-eating episodes $\geq 70\%$ by the fourth week of treatment was applied in order to determine rapid response as previously done in the literature.

These three classification methods were then evaluated in terms of their ability to predict treatment outcome at end of treatment and follow-up. χ^2 analyses were used to analyze binge-eating remission and φ was calculated as a measure of effect size (small: ≥ .10; medium: ≥ .30; large: ≥ .50). Generalized estimating equation (GEE) models based upon a negative binomial distribution were used for binge-eating frequency. Mixed-effects linear models with random intercepts were used for symmetrical continuous outcomes (BDI, BMI). Models included main effects for class (based on the three methods described above), time (pretreatment, posttreatment, 6-month follow-up, 18-month follow-up; results not reported here, cf. de Zwaan et al., 2017), and Class × Time interaction. Missing data for binge-eating remission or frequency, depression, and BMI were present in 0.0 ± 0.0% of patients at pretreatment, 1.9 ± 0.7% at posttreatment, 7.8 ± 1.8% at 6-month follow-up, and 32.6 ± 1.6% at 18-month follow-up.

Missing data were handled using maximum likelihood. For sensitivity analysis, the results from the predictor analysis were compared with those based on multiple imputation, where parameter estimates were pooled across five imputed data sets. The results from the predictor analyses based on multiple imputation were reported only in case of differences in significance of effects. Finally, the three classification methods were compared regarding their consistency using χ^2 analyses. A two-tailed α of .05 was applied to all statistical tests.

Results

Early Change Trajectories of Binge Eating

Evaluating LGMM models with 1-5 classes, BIC and cAIC were lowest for a four-class solution (Table 1); thus, the four-class model was selected as the best fitting model of early change in binge eating (Table 2). Graphically, Class 1, revealing persistent binge eating at a low level, was named *Low level binge eating stable* (Figure 1). Classes 2, 3, and 4 were characterized

by decreasing binge eating starting from varying baseline levels. These classes were named *Low* (Class 2), *Medium* (Class 3), and *High level binge eating decreasing* (Class 4). Class 1 assembled the largest number of patients (47.8%, 41/86), while only three patients (3.5%) belonged to Class 4 *High level binge eating decreasing* (Table 2). Because of the low number of patients assigned to this class, Class 4 was excluded from the following analyses.

As depicted in Figure 1, patients from Class 1 *Low level binge eating stable* showed an almost persistent or slightly reduced binge eating from an average of 2.66 weekly binge-eating episodes at pretreatment to 1.63 at week 4; those from Class 2 *Low level binge eating decreasing* presented a reduction from 2.05 to 0.11 episodes; and those from Class 3 *Medium level binge eating decreasing* revealed a decrease from 6.15 to 3.12 episodes. Further, the early change trajectories of binge eating graphically appeared to extend over weeks 5 to 16 of treatment.

The three-class model significantly predicted binge-eating remission at 6-month follow-up, $\chi^2(df = 2, N = 81) = 9.19$, $p = .010$, $\varphi = .34$, but not at posttreatment or 18-month follow-up, $\chi^2(df = 2) = 1.95, 4.53$, both $p > .05$, $\varphi = .16, .24$. In post-hoc tests, remission rates at 6-month follow-up were significantly higher ($p < .05$) for Class 1 *Low level binge eating stable* and Class 2 *Low level binge eating decreasing* compared to Class 3 *Medium level binge eating decreasing*.

Regarding the secondary outcomes, significant effects of Class and Class × Time were found for binge-eating frequency, both $p < .05$. Follow-up analyses across timepoints revealed a significantly lower binge-eating frequency in Class 2 *Low level binge eating decreasing* than in Class 1 *Low level binge eating stable*, and both classes showed a significantly lower binge-eating frequency than Class 3 *Medium level binge eating decreasing* (all $p < .05$; Table A2, Appendix). At pretreatment and 6-month and 18-month follow-ups, patients in Class 1 *Low level binge eating stable* and Class 2 *Low level binge eating decreasing* showed a significantly lower binge-

eating frequency than those in Class 3 *Medium level binge eating decreasing* (all $p < .05$). In addition, at 6-month follow-up those in Class 2 reported a significantly lower binge-eating frequency than those in Class 3 ($p < .05$). Classes did not differ in binge-eating episodes at posttreatment (all $p > .05$). Patients in each class significantly reduced their binge eating from baseline to posttreatment (all $p < .001$). Those in Class 2 *Low level binge eating decreasing* experienced a further significant decrease in binge eating from posttreatment to 6-month follow-up and another increase from 6-month follow-up to 18-month follow-up (both $p > .05$). Patients in Class 1 and Class 3 remained unchanged from posttreatment to 18-month follow-up (both $p > .05$). There were no significant effects of the three-class model on depression and BMI, all $p > .05$.

Rapid Response in Binge Eating

The ROC analysis on the number of binge-eating episodes over the past seven days of each of the first four weeks of treatment regarding posttreatment binge-eating remission revealed a significant result at week 1 ($AUC = .647$, $SE = .060$, $p = .024$), but not at weeks 2 through 4 (AUC: .478 - .559, SE .063 - .065, all $p > .05$). A reduction in binge eating at week 1 of ≥ 10% had the highest sensitivity (.627) and specificity (.636), and was therefore used as a cut-off to determine Week 1 Rapid Response. Using this cut-off, Week 1 Rapid Response was identified in 52.4% (44/84) of patients. At posttreatment, week 1 rapid responders had significantly higher rates of binge-eating remission than non-rapid responders [72.7% (32/44) vs. 47.5% (19/40); $\chi^2(df = 1) = 5.59$, $p = .018$, $\varphi = .26$], but not at 6-month follow-up [59.1% (26/44) vs. 47.5% (19/40); $\chi^2(df = 1) = 1.13$, $p = .287$, $\varphi = .12$], nor at 18-month follow-up [38.6% (17/44) vs. 25.0% (10/40); $\chi^2(df = 1) = 1.79$, $p = .181$, $\varphi = .15$]. There were no significant effects of Week 1

Rapid Response or Week 1 Rapid Response × Time on the secondary outcomes (all $p > .05$; Table 4).

As the results of the ROC analysis differed from those reported in the literature, rapid response was additionally defined as ≥ 70% reduction in the number of binge-eating episodes at week 4 (Grilo et al., 2012). Using this cut-off, Week 4 Rapid Response was identified in 38.1% (32/84) of patients and did not predict binge-eating remission at either timepoint [posttreatment: 68.8% (22/32) vs. 55.8% (29/52); 6 months: 53.1% (17/32) vs. 53.8% (28/52); 18 months: 37.5% (12/32) vs. 28.8% (15/52); $\chi^2(df = 1) = 0.04 - 1.40$, all $p > .05$, $\varphi = .01 - .13$]. There were no significant effects of Week 4 Rapid Response or Week 4 Rapid Response × Time on binge-eating frequency (both $p < .05$), however, there was a significant effect of Week 4 Rapid Response on depression ($p < .05$; Table 4), indicating that week 4 rapid responders overall reported lower depression than week 4 non-rapid responders (Table A1 Appendix), but no further significant main or interaction effects with time emerged on any of the secondary outcomes (all $p > .05$).

Consistency of Early Change Trajectories and Rapid Response Classifications

When examining the consistency of early change trajectories (Classes 1 to 3) and Week 1 Rapid Response classifications, there was no significant difference between them, $\chi^2(df = 2, N = 81) = 1.08$, $p = .583$, $\varphi = .12$. Thus, no early change trajectory was characterized by Week 1 Rapid Response more than others (Table 4). In contrast, when analyzing the consistency of early change trajectories and Week 4 Rapid Response classifications, there was a significant difference, $\chi^2(df = 2, N = 81) = 16.36$, $p < .001$, $\varphi = .45$. Class 1 *Low level binge eating stable* revealed a significantly lower proportion of week 4 rapid responders than non-rapid responders,

while Class 2 *Low level binge eating decreasing* revealed a higher proportion of week 4 rapid responders than non-rapid responders (both post-hoc $p < .01$).

Discussion

In this first LGMM analysis of early change trajectories in CBT of full and subsyndromal BED, we identified three latent classes of change in binge eating during the first four weeks of treatment. In predictor analyses, this classification was predictive of remission from binge eating at 6-month follow-up: Patients with *Low level binge eating stable* or *decreasing* displayed higher binge-eating remission than patients with *Medium level binge eating decreasing*. In addition, their binge-eating frequency was lower at 6-month and 18-month follow-up, and those with *Low level binge eating decreasing* reported a lower binge-eating frequency than those with *Low level binge eating stable* at 6-month follow-up. Thus, consistent with our hypotheses, early change trajectories significantly predicted binge-eating outcome at follow-up, whereas no significant effect was observed at post-treatment. Those with the lowest initial level of binge eating and an early decrease did best, while stable binge eating over treatment and, in particular, higher baseline levels of binge eating indicated a less favorable outcome.

These results are in contrast with previous rapid response studies highlighting a predictive value of rapid response for binge-eating outcome irrespective of the baseline level of binge eating (Grilo et al., 2006, 2012; Hilbert et al., 2015; Safer & Joyce, 2011; Zunker et al., 2010). In addition, rapid response showed significant associations with binge-eating remission at posttreatment, but inconsistent associations with longer-term remission (Grilo et al., 2012; Hilbert et al., 2015; Safer & Joyce, 2011), which is likely to be inherent to the definition of rapid response using posttreatment remission from binge eating as a criterion in ROC analyses (Grilo et al., 2006, 2012). The early change trajectories in this study were derived from a latent

classification of the course of binge eating over the first four weeks of treatment, which may reflect response patterns of patients with relevance for longer-term outcome, for example, including the ability or motivation to realize changes outside from therapy (Vall & Wade, 2015).

In line with this interpretation, while patients with *Low level binge eating stable* and *Low* or *Medium level binge eating decreasing* presented a significant reduction in binge-eating episodes from pretreatment to posttreatment, where no differences by class were observed, there was some indication of a differential course of binge eating afterwards, in that patients with *Low level binge eating decreasing* showed a further significant improvement in binge-eating frequency from posttreatment to 6-month follow-up and a significant deterioration from 6-month to 18-month follow-up, whereas for patients from the other classes, binge-eating outcome was maintained over follow-up. Latent change trajectories had thus relevance for predicting longer-term binge-eating outcome and course, but early change trajectories did not significantly predict outcome in depression or BMI, which is in accordance with our expectation based on inconsistent associations with non-specific eating disorder outcomes (Linardon et al., 2016).

Overall, the results suggest that both a lower level of initial binge eating and an early decrease over the first weeks of treatment matter in the prediction of better longer-term eating disorder outcome in CBT of BED. Our results suggest that the focus on rapid response irrespective of the baseline level of binge eating, as previously done (Grilo et al., 2006, 2012; Hilbert et al., 2015; Safer & Joyce, 2011; Zunker et al., 2010), risks overlooking prognostically significant differences between classes with an early decrease at different levels of binge-eating symptomatology, for example, between patients with *Low* versus *Medium level binge-eating decreasing*. In fact, we found small-to-medium effect sizes of prediction of binge-eating remission for the early change trajectories ($\varphi = .16 – .34$) that appear to be consistent with those

from a meta-analysis on rapid response of BED on diverse CBT studies (r = .21 – .27; Linardon et al., 2016). However, in the direct comparison of diverse classification methods of early treatment-related change in our study, effect sizes in the prediction of binge-eating remission for the early change trajectories were greater than those for the "conventional" rapid response classifications (φ = .01 – .26).

In addition, the classifications were only partially consistent. Using Grilo et al.'s definition (2012) of rapid response as a ≥ 70% reduction in binge eating at week 4, patients with *Low level binge eating decreasing* were predominantly rapid responders, while those with *Low level binge-eating stable* were predominantly non-rapid responders. In contrast, patients with *Medium level binge eating decreasing* did not differ by rapid or non-rapid response. Unlike the LGMM-based classification, rapid response was neither significantly predictive of binge-eating remission, nor of binge-eating frequency. Both outcomes are, however, considered to be core criteria of treatment success in most clinical studies of BED (Brownley et al., 2016; Vocks et al., 2010). Notwithstanding, rapid response significantly predicted lower depression across timepoints, suggesting it to be a predictor of psychopathology rather than of binge-eating behavior, which was similarly found in two previous studies of high-intensity, individual specialist treatments that used retrospective within-treatment assessment of binge eating (Hilbert et al., 2015; Zunker et al., 2010), but not in another study using therapist-reviewed daily self-monitoring of binge eating (Grilo et al., 2012). Thus, the prognostic significance of rapid response may be influenced by assessment methods and their specific biases (e.g., retrospective recall bias versus self-monitoring correction through non-blinded therapist review). Overall, retrospective recall of binge eating through the EDE-Q as used for within-treatment assessment

of binge eating in this study, was found to have acceptable convergence with interview (EDE) and self-monitoring (Grilo, Masheb, & Wilson, 2001a, b).

In contrast to the definition of rapid response as ≥ 70% reduction in binge eating at week 4 (Grilo et al., 2012), the ROC analysis-based classification of rapid response as a week 1 reduction in binge eating ≥ 10%, did not significantly map onto the LGMM-based classification of early change trajectories. Consistent with studies investigating rapid response in specialist treatments that used retrospective within-treatment assessment of binge eating (Hilbert et al., 2015; Zunker et al., 2010) or pure self-monitoring (Safer & Joyce, 2011), but in contrast with other studies using therapist-reviewed self-monitoring (Grilo et al., 2006, 2012), this study's ROC analysis did not lead to a solution with satisfying sensitivity and specificity. The identified cutoff of ≥ 10% reduction in binge eating at week 1 resembled the definition of ≥ 15% reduction in binge eating at week 1 in the Zunker et al. (2010) study. This earlier and lower cutoff may be specific to CBT, as our study and the study by Zunker et al. (2010) determined rapid response in CBT only, whereas the other studies determined rapid response in aggregated ROC analyses of CBT and BWL or antidepressant medication (and/or placebo conditions; Grilo et al., 2006, 2012). The CBT-inherent focus on improving binge eating in the early treatment phase (Fairburn, 2008; Hilbert & Tuschen-Caffier, 2010) may have fostered the very early responses. In addition, this study offered a high frequency of individual sessions early in treatment (two sessions per week in month 1), so that substantial changes may have occurred already during the first week of treatment. It is of note, however, that in our and Zunker et al.'s (2010) study, the early and low cutoff of binge-eating reduction had little prognostic value for binge-eating remission beyond posttreatment, and further treatment outcomes were also not predicted. More research is warranted on the within-treatment binge eating assessment considering new or

combined methods (e.g., ecological momentary assessment, session-wise retrospective assessment) in order to enhance the predictive validity of rapid response for individual clinical decision-making.

Among the strengths of this fine-grained analysis of early change trajectories are the reliance on a multicenter randomized-controlled trial of CBT for full and subsyndromal BED with high internal validity in design and conduct for limiting systematic bias (Brauhardt et al., 2014; de Zwaan et al., 2012, 2017). Limiting generalizability, this study's sample was mostly female and well-educated, and the body mass index was required to fall within the overweight to obese range (27.0 – 40.0 kg/m^2; de Zwaan et al., 2017). Further, future LGMM analyses should shed light on whether the early change trajectories identified for CBT apply to other interventions as well. Maximum likelihood was used to accommodate missing data. As a sensitivity analysis, LGMM and predictor analyses were repeated using multiple imputation for handling missing data. The classification of early change trajectories and the significance of predictive effects did not change, suggesting that the results were not substantially affected by missing data.

Although the sample size in the CBT arm was sufficiently large for the LGMM analyses ($N = 89$) and a bootstrap procedure was performed selecting 200 consecutive random samples of the original sample, future investigation of latent change trajectories should preferably use larger sample sizes, in order to replicate this study's results, address not only early, but also later change trajectories (e.g., Owen et al., 2015; Stulz, Gallop, Lutz, Wrenn, & Crits-Christoph, 2010; Stulz, Thase, Klein, Manber, & Crits-Christoph, 2010; Thibodeau et al., 2015), and allow for the inclusion of cubic components in LGMM, suited to capture latent figures of both sudden gains and losses (Lutz, Ehrlich & Rubel, 2013; Ehrlich & Lutz, 2015). In addition, a replication

in a larger sample could offer further insight into the course of patients with a high initial level of binge eating; in this study, the class with *High level binge eating decreasing* had to be excluded from the predictor and consistency analyses because of the low number of patients assigned to this class (Class 4, $n = 3$). The overall sample size provided only limited power to identify significant predictors of treatment outcome. However, it is of note that six of the conducted 27 predictor analysis tests were significant and the percentage of significant findings (22.2%) exceeded that of significant effects to be expected by chance (5%).

Regarding clinical utility, the results underline the necessity to monitor early trajectories of binge eating within CBT. We found early change trajectories determined by LGMM to improve the prediction of treatment outcome when compared to "conventionally defined" rapid response, which has been considered to be the most robust predictor of treatment outcome in the eating disorders, including BED (Vall & Wade, 2015). Responders and non-responders in early change trajectories (i.e., patients with versus without binge-eating remission) showed a 43.0% difference in rates of binge-eating remission averaged across posttreatment and follow-up, with the lowest discrepancy in patients with *Low level binge eating stable* (20.3%), and the highest discrepancies in those with *Medium* (33.4%) and *Low level binge eating decreasing* (40.3%; Figure 2, Table 3). This underlines the clinical utility of examining patterns of early change in general and assigns the greatest predictive value to trajectories characterized by early decreases and higher initial levels of binge eating in particular. In contrast, the respective figures were 21.7% for the rapid response classification based on a 70% reduction in binge eating at week 4, and 24.4% for the rapid response classification based on a 10% reduction in binge eating at week 1.

While LGMM allows for an in-depth examination of latent change trajectories, notwithstanding, this method is unlikely to be applicable in clinical practice. Rather, based on this study's results, future research on early change trajectories may identify and confirm slope indicators and/or thresholds of within-treatment change in binge eating, helping clinicians to identify patients likely to show non-response after treatment as early as possible. As an approach to this aim, clinicians could use this study's results and compare the binge-eating frequency of their patients to the average binge-eating frequency of the latent change trajectories over the first weeks of treatment in order to determine the most likely class assignment, derive prognostic information, and potentially adapt their therapeutic strategy.

Although they showed notable early reductions in binge eating, patients with greater initial binge-eating frequency were found to deserve particular clinical attention. Further, among the patients with low initial binge-eating frequency, those who did not show a substantial improvement over the first four weeks of treatment were likely to maintain at the end of treatment a binge-eating frequency close to the DSM-5 diagnostic threshold of one episode of binge eating per week (APA, 2013; Figure 1). These patients may benefit from further adapting CBT to their needs, for example, through a greater intensity of treatment, identification and management of the individually relevant maintenance factors, and indicated use of adjunctive interventions (e.g., Turton, Bruidegom, Cardi, Hirsch, & Treasure, 2016). Additional evidence may inform about interventions suited to achieve and improve early therapeutic gains.

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Table 1

Latent Growth Mixture Modeling of Binge Eating over the First Four Weeks of Treatment: Model Fit Indices (N = 86)

Classes	*BIC*	*aBIC*	*cAIC*	*AIC*	*LL*
1	2123.22	2113.76	2126.22	2115.86	-1054.93
2	1790.92	1768.83	1797.91	1773.73	-879.87
3	1672.73	1638.03	1683.73	1645.73	-811.87
4	**1668.35**	1621.03	**1683.35**	1631.54	-800.77
5	1674.04	**1614.09**	1693.04	**1627.40**	**-794.70**

Note. Minimum value for each fit index is bolded. *BIC* = Bayesian information criterion; *aBIC* = sample size-adjusted Bayesian information criterion; *cAIC* = consistent Akaike information criterion; *AIC* = Akaike information criterion; *LL* = log likelihood.

Table 2

Four-Class Latent Growth Mixture Model of Binge Eating over the First Four Weeks of Treatment: Description, Class Membership, and Parameter Estimates

			Intercept		Linear		Quadratic	
Class	Description	n	Estimate (*SE*)	*p*	Estimate (*SE*)	*p*	Estimate (*SE*)	*p*
1	*Low level binge eating stable*	41	0.98 (0.13)	<.001	-0.36 (0.13)	.006	0.06 (0.04)	.134
2	*Low level binge eating decreasing*	19	0.72 (0.30)	.016	-0.48 (0.29)	.094	-0.06 (0.08)	.458
3	*Medium level binge eating decreasing*	23	1.82 (0.13)	<.001	-0.28 (0.11)	.013	0.03 (0.03)	.318
4	*High level binge eating decreasing*	3	3.05 (0.10)	<.001	-0.17 (0.20)	.383	-0.03 (0.07)	.708

Table 3

Primary and Secondary Outcomes by Early Change Trajectories

		Pretreatment		Posttreatment		6-month Follow-up		18-month Follow-up	
		N / M	*% / SD*	*N / M*	*% / SD*	*N / M*	*% / SD*	*N / M*	*% / SD*
Class 1 *Low level binge*	Binge-eating remission	0	0.0	26	63.4	26	63.4	19	46.3
eating stable	Binge-eating frequency	15.27	10.16	1.66	3.12	2.39	4.73	3.71	6.18
(*n* = 41)	Depression	11.98	8.05	8.76	10.94	8.97	9.50	8.27	7.67
	Body mass index	34.86	3.69	34.86	4.31	33.99	4.10	34.75	4.94
Class 2 *Low level binge*	Binge-eating remission	0	0.0	14	73.7	15	78.9	8	42.1
eating decreasing	Binge-eating frequency	10.89	8.43	0.95	1.99	0.42	1.07	2.63	3.18
(*n* = 19)	Depression	7.79	6.69	5.72	8.86	5.82	8.55	4.68	8.07
	Body mass index	34.12	4.12	33.73	4.94	33.12	5.17	33.95	4.73
Class 3 *Medium level*	Binge-eating remission	0	0.0	11	52.4	7	33.3	4	19.0
binge eating decreasing	Binge-eating frequency	28.05	14.97	4.71	9.81	6.38	8.08	8.57	8.70
(*n* = 23)	Depression	14.38	9.90	10.58	11.50	11.57	11.33	5.77	12.21
	Body mass index	33.74	3.92	33.52	4.61	33.47	4.98	33.38	4.76

Note. Binge-eating remission (zero objective binge-eating episodes) and binge-eating frequency (number of objective binge-eating episodes) over the past 28 days assessed through the Eating Disorder Examination. Depression, operationalized through the sum score, of the Beck Depression Inventory (0 to 63, with higher scores indicating greater severity). Body mass index, kg/m^2, derived from measured body weight and height.

Table 4

Main Effects of Class and Interaction Effects with Time for Early Change Trajectories, Week 1 Rapid Response, and Week 4 Rapid Response on Outcomes of Binge-Eating Disorder

		Main Effect			Interaction		
Outcomes	Test	Test Statistic	*df*	*p*	Test Statistic	*df*	*p*
Early Change Trajectories							
Binge-eating frequency	Wald χ^2	26.48	2	< .001	14.07	6	.029
Depression	F	1.97	2, 79	.147	1.25	6, 145	.285
Body mass index	F	0.59	2, 81	.558	0.43	6, 98	.433
Week 1 Rapid Response							
Binge-eating frequency	Wald χ^2	0.38	1	.538	5.97	3	.113
Depression	F	0.81	1, 84	.371	2.30	3, 151	.079
Body mass index	F	0.03	1, 84	.873	0.37	3, 108	.775

Table 4 (continued)

		Main Effect			Interaction		
	Test	Test Statistic	*df*	*p*	Test Statistic	*df*	*p*
Week 4 Rapid Response							
Binge-eating frequency	Wald χ^2	0.66	1	.416	2.21	3	.530
Depression	F	6.80	1, 84	.011	0.24	3, 153	.866
Body mass index	F	0.01	1, 84	.916	0.78	3, 107	.506

Note. Generalized Estimating Equations analyses and mixed model analyses of Early Response × Time (pretreatment, posttreatment, 6-month follow-up, 18-month follow-up). Binge-eating frequency over the past 28 days assessed through the Eating Disorder Examination. Depression assessed through the Beck Depression Inventory. Body mass index, kg/m^2, derived from measured body weight and height.

Table 5

Concordance between Early Change Trajectories and Week 1 and Week 4 Rapid Response

Classes		Week 1			Week 4		
		Rapid Response	Non-rapid response	Total	Rapid Response	Non-rapid response	Total
Class 1 *Low level binge eating stable*	n	21	20	41	8[a]	33[b]	41
	%	51.2%	48.8%	100.0%	19.5%	80.5%	100.0%
Class 2 *Low level binge eating decreasing*	n	12	7	19	14[a]	5[b]	19
	%	63.2%	36.8%	100.0%	73.7%	26.3%	100.0%
Class 3 *Medium level binge eating*	n	10	11	21	8	13	21
decreasing	%	47.6%	52.4%	100.0%	38.1%	61.9%	100.0%
Total	n	44	40	84	32	52	84
	%	52.4%	47.6%	100.0%	38.1%	61.9%	100.0%

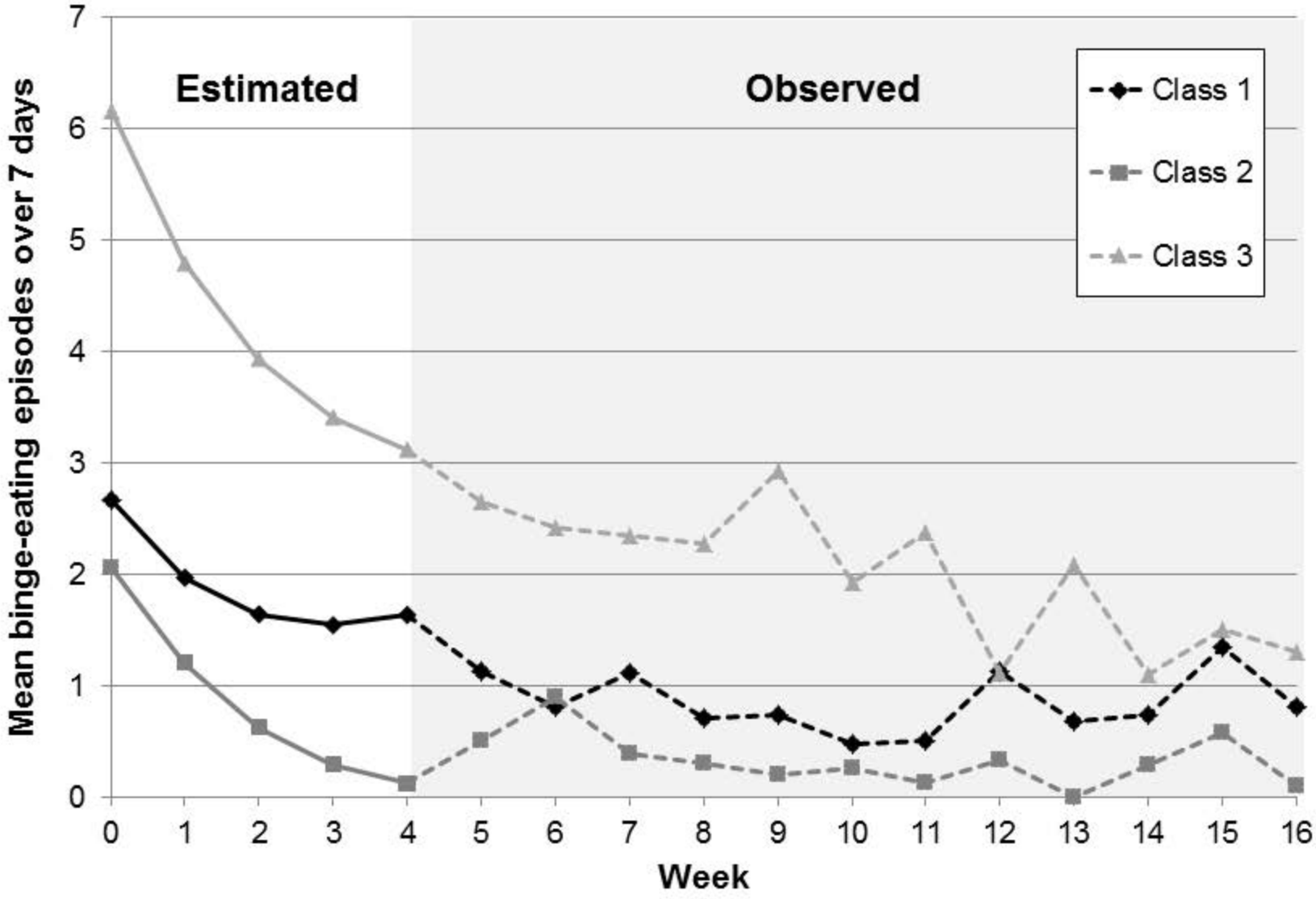
Note. [a,b]different superscripts indicate significant post-hoc within-class differences between rapid response and non-rapid response.

$p < .01$

Figure Captions

Figure 1. Estimated early change trajectories of binge eating over the first four weeks of treatment and observed binge eating over the fifth to sixteenth week of treatment. Estimation through Latent Growth Mixture Modeling. Class 1 *Low level binge eating stable* (*n* = 41); Class 2 *Low level binge eating decreasing* (*n* = 19); Class 3 *Medium level binge eating decreasing* (*n* = 23).

Figure 2. Remission from binge eating at posttreatment, 6-month follow-up, and 18-month follow-up by early change trajectories of binge eating over the first four weeks of treatment. Class 1 *Low level binge eating stable* (*n* = 41); Class 2 *Low level binge eating decreasing* (*n* = 19); Class 3 *Medium level binge eating decreasing* (*n* = 23).


Estimated
Observed
Class 1
Class 2
Class 3
Mean binge-eating episodes over 7 days
Week
0
1
2
3
4
5
6
7
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

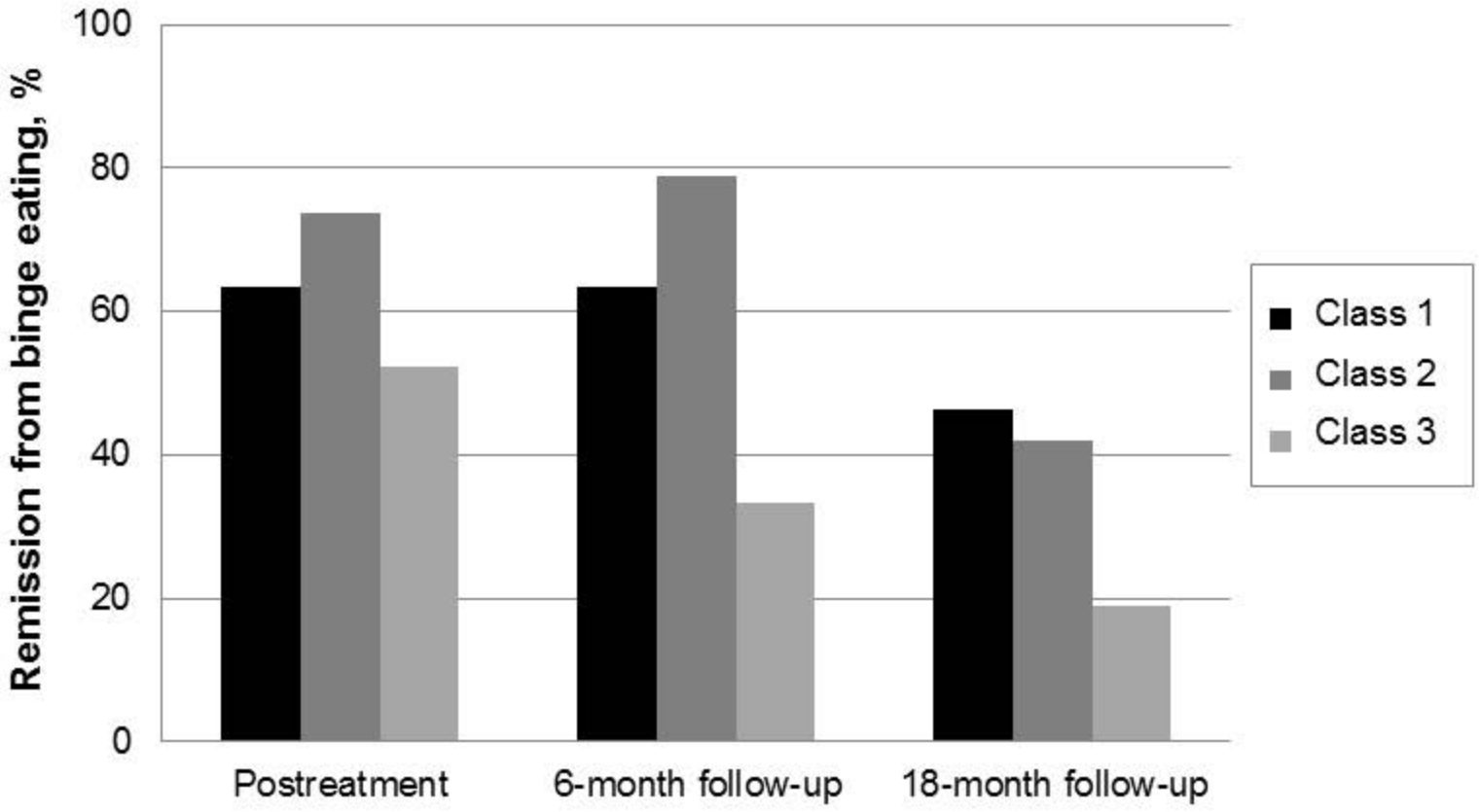

Remission from binge eating, %
100
80
60
40
20
0
Postreatment
6-month follow-up
18-month follow-up
Class 1
Class 2
Class 3

Table A1

Parameter Estimates for Follow-up Analyses on Continuous Outcomes

Comparison	Estimate	*SE*	*df*	*p*	95% CI
Early Change Trajectories: Binge-Eating Frequency					
Class 1 vs. Class 2	2.03	0.91	1	.026	0.24 – 3.82
Class 1 vs. Class 3	-5.35	1.87	1	.004	-9.02 – -1.68
Class 2 vs. Class 3	-7.38	1.78	1	< .001	-10.87 – -3.90
Class 1: Pretreatment vs. Posttreatment	13.61	1.44	1	< .001	10.79 – 16.43
Class 1: Posttreatment vs. 6-month Follow-up	-0.73	0.64	1	.253	-1.99 – 0.52
Class 1: 6-month Follow-up vs. 18-month Follow-up	-1.32	0.69	1	.056	-2.67 – 0.03
Class 2: Pretreatment vs. Posttreatment	9.95	1.95	1	< .001	6.13 – 13.77
Class 2: Posttreatment vs. 6-month Follow-up	0.53	0.25	1	.036	0.03 – 1.02
Class 2: 6-month Follow-up vs. 18-month Follow-up	-2.21	0.72	1	.002	-3.61 – -0.81
Class 3: Pretreatment vs. Posttreatment	23.33	3.33	1	< .001	16.80 – 29.87
Class 3: Posttreatment vs. 6-month Follow-up	-1.67	2.55	1	.513	-6.66 – 3.32
Class 3: 6-month Follow-up vs. 18-month Follow-up	-2.19	2.28	1	.336	-6.65 – 2.27

Table S1 (continued)

Comparison	Estimate	*SE*	*df*	*p*	95% CI
Pretreatment: Class 1 vs. Class 2	4.37	2.45	1	.074	-0.43 – 9.17
Pretreatment: Class 1 vs. Class 3	-12.78	3.55	1	< .001	-19.74 – -5.82
Pretreatment: Class 2 vs. Class 3	-17.15	3.70	1	< .001	-24.41 – -9.90
Posttreatment: Class 1 vs. Class 2	0.71	0.65	1	.277	-0.57 – 1.99
Posttreatment: Class 1 vs. Class 3	-3.06	2.14	1	.154	-7.26 – 1.15
Posttreatment: Class 2 vs. Class 3	-3.77	2.14	1	.078	-7.95 – 0.42
6-month Follow-up: Class 1 vs. Class 2	1.97	0.77	1	.010	0.47 – 3.47
6-month Follow-up: Class 1 vs. Class 3	-3.99	1.87	1	.033	-7.65 – -0.33
6-month Follow-up: Class 2 vs. Class 3	-5.96	1.74	1	.001	-9.36 – -2.56
18-month Follow-up: Class 1 vs. Class 2	1.08	1.19	1	.366	-1.25 – 3.41
18-month Follow-up: Class 1 vs. Class 3	-4.86	2.08	1	.020	-8.95 – -0.78
18-month Follow-up: Class 2 vs. Class 3	-5.94	1.98	1	.003	-9.83 – -2.05
Week 4 Rapid Response: Depression	4.41	1.69	84	.011	1.05 – 7.77

Notes. Follow-up analyses for the generalized estimating equations and mixed linear model analysis of Class (or Rapid Response) × Time. Class 1 *Low level binge eating stable* (*n* = 41); Class 2 *Low level binge eating decreasing* (*n* = 19); Class 3 *Medium level binge*

eating decreasing (*n* = 23). Binge-eating frequency over the past 28 days assessed through the Eating Disorder Examination. depression assessed through the Beck Depression Inventory (0-63). Pretreatment, posttreatment, and 6- and 18-month follow-up assessments.