A 1-year follow-up study of the longitudinal interplay between emotion dysregulation and childhood trauma in the treatment of anorexia nervosa

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Abstract
Objective: The study aimed to investigate the complex relationship between eating disorder (ED) specific psychopathology, emotion dysregulation, and their longitudinal variations in patients with anorexia nervosa (AN) treated with a multidisciplinary approach including enhanced cognitive-behavior therapy (CBT-E), and to provide an integrated model which includes childhood trauma as a predictor of worse treatment outcomes.

Method: In total, 120 female patients with AN were evaluated at admission (T0), and 105 were re-evaluated after 1 year (T1) of treatment. At T0, patients underwent a clinical assessment and filled the Symptom Checklist 90-Revised (SCL90-R), the Eating Disorders Examination Questionnaire (EDE-Q), the Difficulties in Emotion Regulation Scale (DERS), and the Childhood Trauma Questionnaire (CTQ). SCL-90-R, EDE-Q, and DERS were readministered at T1. Variations between T0 and T1 were evaluated, and the proposed model was investigated using bivariate latent change score analysis in a structural equation modeling (SEM) framework.

Results: An overall significant clinical amelioration was observed after treatment. A unidirectional effect of DERS scores on EDE-Q variations was outlined by SEM: patients with higher baseline DERS scores achieved less EDE-Q improvements, and EDE-Q latent change score was significantly predicted by longitudinal variations of DERS—but not vice versa. Higher CTQ scores predicted reduced treatment efficacy for ED-specific psychopathology through the mediating effect of higher baseline DERS scores.

Discussion: The present study sheds light on the mechanism by which early trauma compromises treatment outcome in patients with AN, underlining the crucial role of emotional dysregulation.
1 | INTRODUCTION

Anorexia nervosa (AN) is a clinically heterogeneous condition associated with a wide range of negative outcomes, including severe medical consequences, an elevated risk of chronicity, and one of the highest mortality rates among psychiatric disorders (5–10%) (Jagielska & Kacperska, 2017; Klump, Bulik, Kaye, Treasure, & Tyson, 2009). A significant percentage of patients with AN have a poor prognosis, with less than half achieving full recovery overall (Steinhausen, 2009). For this reason, investigating the role of specific psychopathological features as potential targets of psychological interventions in treatment programs might prove useful to better define the prognostic implications for these patients.

In this perspective, emotion dysregulation is a key aspect of eating disorders (EDs), regardless of diagnostic subtypes (Lavender et al., 2015; Mallorquí-Bagué et al., 2018; Monell, Clinton, & Birgegård, 2018). According to Gratz and Roemer’s (2004) model, emotion dysregulation can be conceptualized through four different dimensions: (a) the use of maladaptive strategies to modulate emotions; (b) a reduced competence to maintain control when distressed; (c) an impaired ability to undergo distressing experiences to pursue meaningful activities; and (d) a lack of emotional awareness, clarity, and acceptance. A recent review by Lavender et al. (2015) suggested that individuals with AN display deficits in each of these domains of emotion regulation.

Difficulties in emotion regulation are closely related to the presence of previous traumatic experiences—particularly those experienced during childhood—and this association plays a key role in explaining the development of subsequent psychiatric disorders (Dunn, Nishimi, Gomez, Powers, & Bradley, 2018; Dvir, Ford, Hill, & Frazier, 2014). Preliminary data from cross-sectional studies in EDs seem to support this hypothesis, with emotion dysregulation mediating the relationship between early adversities and ED psychopathology (Moulton, Newman, Power, Swanson, & Day, 2015; Racine & Wildes, 2014). Furthermore, several observations seem to indicate that persons with early trauma represent a distinct population within patients with EDs, in terms of psychopathological characterization (Castellini, D’Anna, et al., 2020; Monteleone et al., 2021; Rodgers et al., 2019) and longitudinal course (Castellini et al., 2018; Castellini, Rossi, et al., 2020; Lelli, Castellini, Cassioli, Monteleone, & Ricca, 2019).

Indeed, emotion dysregulation may play a pivotal role as a predictor of ED treatment outcomes, and it could represent a mediating link between childhood adversities and treatment nonresponse. The only one longitudinal study on this topic reported that emotion dysregulation predicted a reduced improvement in ED psychopathology among patients with AN discharged after intensive hospitalization (Racine & Wildes, 2015). No longitudinal study has investigated the effects of emotion dysregulation on treatment outcome from admission to discharge, and no study has integrated the role of childhood traumatic experiences into this model. Furthermore, despite the strong interest of the scientific community in emotion dysregulation and its established relevance in cross-sectional studies (Haynos & Fruzzetti, 2011; Lavender et al., 2015; Treasure & Schmidt, 2013), experts have noted a remarkable lack of clinical evidence from longitudinal studies (Lavender et al., 2015).

The aim of the present study was to examine a theoretical model in which emotion dysregulation represented a prognostic factor for AN treatment outcome. In particular, the present work tested the hypothesis that, in patients with AN treated with a multidisciplinary approach based on enhanced cognitive behavior therapy (CBT-E) (Dalle Grave, El Ghoch, Sartirana, & Calugi, 2016), changes in emotion dysregulation levels during the treatment period predict subsequent ED psychopathology improvement, with a longitudinal coupling between emotion regulation and clinical amelioration. In addition, this model tested the extent to which childhood trauma indirectly predicted a reduced improvement in ED psychopathology over the course of treatment through higher levels of emotion dysregulation (Figure 1).

2 | METHOD

A consecutive series of female patients who attended the Eating Disorders Clinic of Florence University Hospital for the first time seeking outpatient care was enrolled from January 2019 to April 2021, provided they met the following inclusion criteria: female sex, age between 18 and 65 years, diagnosis of AN according to the...
The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1994), patients and HC. The following self-reported questionnaires were administered to both standardized calibrated instruments. Immediately after the clinical evaluation, using the Structured Clinical Interview for DSM-5 Disorders with expert psychiatrists (authors G.C. and V.R.) and medical evaluation, the assessment was conducted by means of a face-to-face interview with the current International Conference on Harmonization of Technical Requirements for Good Clinical Practice guidelines, as contained in the Declaration of Helsinki of 1964 and its later amendments.

2.1 Baseline assessment

The assessment was conducted by means of a face-to-face interview with expert psychiatrists (authors G.C. and V.R.) and medical evaluation, using the Structured Clinical Interview for DSM-5 Disorders (First et al., 2016). Body mass index (BMI) was evaluated using standard calibrated instruments. Immediately after the clinical evaluation, the following self-reported questionnaires were administered to both patients and HC.

- The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1994), an assessment of different psychopathological areas through 90 items on a five-point scale; the average of all items, called Global Severity Index (GSI), was used as an overall measure of psychopathology, and showed good reliability (Cronbach’s \( \alpha = .98 \)).
- The Eating Disorder Examination Questionnaire (EDE-Q 6.0) (Calugi et al., 2016) provides four subscales ranging from 0 to 6 assessing ED-specific psychopathology (Dietary Restraint, Eating Concern, Weight Concern, Shape Concern), and a Total Score (obtained by averaging all subscales) with excellent reliability (Cronbach’s \( \alpha = .97 \)).
- The Difficulties in Emotion Regulation Scale (DERS) (Gratz & Roemer, 2004) evaluates trait-level emotion dysregulation through 36 items on a five-point scale. Six subscales (Non-Acceptance of Emotional Responses, Difficulties Engaging in Goal-Directed Behavior, Limited Access to Emotion Regulation Strategies, Impulse Control Difficulties, Lack of Emotional Clarity, and Lack of Emotional Awareness) can be obtained from the sum of the appropriate items, and sum of all items yield a Total Score (Cronbach’s \( \alpha = .89 \)).
- The 28-item version of the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003) investigates self-reported experiences of maltreatment during childhood on a five-point scale. Items can be summed to obtain a Total Score (Cronbach’s \( \alpha = .71 \)) and five subscales (Emotional Neglect, Emotional Abuse, Sexual Abuse, Physical Neglect, and Physical Abuse).

The diagnostic procedures and the psychometric tests described are part of the clinical routine performed at our outpatient facility.

2.2 Treatment and follow-up

Patients attended regular outpatient evaluations from expert psychiatrists and dieticians for 12 months and were treated with CBT-E (Fairburn, 2008). All patients were provided with at least 40 individual psychotherapy sessions over the treatment period (median number of sessions = 42). Following standard CBT-E protocol, sessions were initially administered weekly, while in the last phase they were scheduled with a frequency of one every two or three weeks, depending on individual needs (Fairburn, 2008).

These interventions were part of the clinical routine of the organizing center, and they were in no way influenced by enrollment in the present study. Patients were evaluated again using SCL-90-R, EDE-Q, and DERS after 1 year (T1), with a maximum margin of 15 days due to organizational and logistical needs.

2.3 Statistics

All continuous variables are reported with means and standard deviations. Baseline comparisons between HCs and patients with AN were performed via age- and BMI-adjusted analyses of covariance (ANCOVA). For patients with AN, linear mixed model analysis with random intercepts and age as a covariate was used to test for significant variations between T0 and T1 measurements.

The complex association between ED-specific psychopathology and emotion dysregulation was investigated by fitting a bivariate Latent Change Score (LCS) model (McArdle, 2009). In univariate LCS analysis, the observed score at a certain timepoint can be modeled as a linear combination of the observed score at the previous timepoint and a change score, which is treated as a latent variable. When the corresponding regression equations are specified in the structural equation modeling (SEM) framework, the intercept and the variance of the subsequent observed score are fixed to zero, whereas both the regression weight on the previous timepoint and the factor loading on the LCS are fixed to one.
(Grimm, Ram, & Estabrook, 2016; Kievit et al., 2018). This particular setup allows the LCS to capture the within-subject variation from one timepoint to the next, which is the outcome of interest of this analysis, and which can be subsequently regressed on other variables. In bivariate LCS models, this technique is applied on two time-varying variables in parallel, which allows for the modeling of complex longitudinal relationships, known as cross-domain coupling (Grimm et al., 2016; Kievit et al., 2018). Hence, these models represent one way to examine both within-subject variation and time-sequential associations between different domains in the context of repeated-measures designs (Grimm et al., 2016). When an LCS is regressed on the previous timepoint, the longitudinal variation of the variable is split into two components: one that depends on the value at the previous timepoint (often called “proportional” effect) and one that does not vary according to the independent variables of the regression equation, which actually corresponds to the intercept of the LCS (called “constant” effect). A significant proportional effect indicates that the higher the value at the previous timepoint, the greater the longitudinal variation. Conversely, a significant constant effect means that at least part of the longitudinal variation is independent of the other variables present in the model.

An initial model was built based on the results of a previous study, where it was shown that the longitudinal trend of the EDE-Q scores was composed of both a constant and a proportional component, whereas that of DERS was only constant, and the coupling was unidirectional (Racine & Wildes, 2015). Assumptions regarding the presence of all effects were tested individually using nested model comparisons (Grimm et al., 2016). With this approach, alternative models are formulated in which the coefficients of interest are fixed or unconstrained one at a time to verify whether, with respect to the initial model, model fit varies in a statistically significant way. This analysis allows to obtain evidence about the actual presence of a hypothesized effect. If a better model emerges, the process can be repeated further by comparing the resulting model with further alternatives until a final model with the best possible fit is reached. A series of trimmed models were created by constraining a specific coefficient to zero, and a chi-square ($\chi^2$) difference test was performed: a statistically significant difference between the trimmed

### TABLE 1  Baseline comparison between patients with anorexia nervosa and healthy controls (age- and BMI-adjusted), performed using analysis of covariance (F values and statistical significance for group differences are reported, together with effect size estimates)

|                | Healthy Controls T0 (n = 81) | Patients with AN T0 (n = 120) | F  | Cohen’s d | Patients with AN T1 (n = 105) | Time effect | Cohen’s d |
|----------------|------------------------------|-------------------------------|----|-----------|-------------------------------|-------------|-----------|
| Age (years)    | 26.04 ± 3.29                 | 25.22 ± 9.55                 | 0.57 | -0.11     | -                             | -           | -         |
| Age of onset (years) | -                          | 17.88 ± 5.01                | -   | 5.05      | -                             | -           | -         |
| BMI (kg/m²)    | 21.07 ± 2.30                 | 16.28 ± 1.40                 | 329.36*** | -2.52     | 18.09 ± 1.78                  | 1.85***     | 1.12      |
| SCL-90-R GSI   | 0.42 ± 0.42                  | 1.52 ± 0.82                  | 119.15*** | 1.69      | 1.02 ± 0.80                   | -0.46***    | -0.69     |
| EDE-Q Dietary Restraint | 0.64 ± 0.86               | 3.38 ± 2.13                  | 117.68*** | 1.69      | 1.66 ± 1.78                   | -1.74***    | -0.97     |
| EDE-Q Eating Concern | 0.41 ± 0.62                | 2.72 ± 1.65                  | 135.85*** | 1.86      | 1.56 ± 1.50                   | -1.14***    | -0.88     |
| EDE-Q Weight Concern | 0.98 ± 0.97                 | 3.29 ± 1.75                  | 115.76*** | 1.64      | 2.24 ± 1.88                   | -0.90***    | -0.62     |
| EDE-Q Shape Concern | 1.30 ± 1.28                 | 3.72 ± 1.84                  | 104.50*** | 1.53      | 2.61 ± 2.01                   | -0.94***    | -0.58     |
| EDE-Q Total Score | 0.83 ± 0.85                  | 3.28 ± 1.70                  | 138.57*** | 1.81      | 2.02 ± 1.72                   | -1.17***    | -0.87     |
| DERS Non-acceptance | 9.96 ± 4.69                 | 16.40 ± 7.62                 | 40.53*** | 1.02      | 13.09 ± 7.53                  | -1.56       | -0.14     |
| DERS Goals     | 12.20 ± 4.63                 | 16.86 ± 5.62                 | 31.59*** | 0.90      | 14.21 ± 5.16                  | -2.13*      | -0.39     |
| DERS Strategies | 15.57 ± 5.69                 | 25.05 ± 8.32                 | 68.22*** | 1.33      | 21.12 ± 8.81                  | -2.15       | -0.23     |
| DERS Impulse   | 8.89 ± 3.82                  | 15.73 ± 6.82                 | 58.22*** | 1.24      | 12.52 ± 7.10                  | -2.76*      | -0.22     |
| DERS Clarity   | 9.66 ± 3.67                  | 15.10 ± 5.98                 | 53.13*** | 1.10      | 12.39 ± 5.74                  | -1.21       | -0.02     |
| DERS Awareness | 6.04 ± 2.79                  | 7.24 ± 3.51                  | 4.48*   | 0.38      | 6.55 ± 3.53                   | 0.07        | 0.16      |
| DERS Total Score | 70.17 ± 20.41              | 106.16 ± 31.03               | 71.82*** | 1.37      | 88.91 ± 33.29                 | -9.83*      | -0.29     |
| CTQ Emotional Neglect | 7.81 ± 3.23                | 10.50 ± 4.55                 | 20.96*** | 0.68      | -                             | -           | -         |
| CTQ Emotional Abuse | 5.57 ± 1.22                | 8.36 ± 4.14                  | 33.71*** | 0.91      | -                             | -           | -         |
| CTQ Sexual Abuse | 5.19 ± 1.18                | 6.24 ± 3.50                  | 6.24*   | 0.40      | -                             | -           | -         |
| CTQ Physical Neglect | 5.49 ± 1.41               | 6.62 ± 2.58                  | 12.38*** | 0.54      | -                             | -           | -         |
| CTQ Physical Abuse | 5.25 ± 1.34                | 5.90 ± 2.67                  | 3.64    | 0.31      | -                             | -           | -         |
| CTQ Total Score | 35.35 ± 8.53              | 45.36 ± 15.77                 | 25.81*** | 0.79      | -                             | -           | -         |

Note: Follow-up data for patients are reported in the right panel, together with longitudinal analyses. *p < .05; ***p < .001.

Abbreviations: AN, anorexia nervosa; BMI, body mass index; CTQ, Childhood Trauma Questionnaire; DERS, Difficulties in Emotion Regulation Scale; EDE-Q, Eating Disorders Examination Questionnaire; M ± SD, mean ± standard deviation; SCL-90-R GSI, Symptom Checklist 90 Revised Global Severity Index.
model and the initial model indicated that the presence of that particular effect considerably improved the fit of the model, and should therefore be retained; otherwise, it should be discarded. In addition to this statistical test, fit indices and whether the elimination made theoretical sense were also considered. Next, a series of unconstrained models were used to test whether each initially constrained effect should instead be freely estimated: a statistically significant difference between the trimmed model and unconstrained model indicated that the unconstrained effect improved the fit of the model and should be retained. All SEM models were assessed by computing the following goodness-of-fit indicators and corresponding general rules for acceptable fit: \( \chi^2 \) test (should be nonsignificant), Comparative Fit Index \((\text{CFI} \geq 0.95 \text{ for good fit})\), Tucker–Lewis Index \((\text{TLI} \geq 0.95 \text{ for good fit})\), Root Mean Square Error of Approximation \((\text{RMSEA} \leq 0.06 \text{ for good fit})\), Standardized Root Mean Square Residual \((\text{SRMR} \leq 0.08 \text{ for good fit})\) (Schreiber, Stage, King, Nora, & Barlow, 2006).

Finally, mediation analysis was performed to test whether CTQ Total Score would predict less improvement in ED-specific psychopathology through higher levels of emotion dysregulation, by computing the 95% bootstrapped confidence interval with 10,000 resamples; the effect was considered statistically significant if the interval did not include zero. To allow a more accurate estimate of the indirect effect, the direct path between CTQ Total Score and EDE-Q was included in the bootstrapped model.

All SEM models were computed on the complete sample of patients \((n = 120)\) using full information maximum likelihood estimation, with robust (Huber–White) standard errors (sandwich estimator). To facilitate model convergence, DERS and CTQ scores were divided by 10 to produce variances more similar to other variables in the model; estimated coefficients should be interpreted accordingly. Standardized regression coefficients (completely standardized solution) were also computed for the final SEM model. All analyses were performed using R (R Core Team, 2020) and the following packages: lavaan (Rosseel, 2012), nlme (Pinheiro et al., 2020).

### RESULTS

At baseline \((T0)\), patients scored higher than HCs on general and ED-specific psychopathology, emotion dysregulation, and childhood trauma, except for CTQ Physical Abuse (Table 1). Baseline data grouped by AN subtype are shown in Table S1, together with comparisons between groups. The initial psychiatric assessment also found that 78 (65.0%) patients also met DSM-5 criteria for concurrent major depressive episode, 76 (63.3%) for an anxiety disorder, 11 (9.2%) for obsessive–compulsive disorder.

Fifteen patients dropped out of treatment, reducing the AN analysis sample to 105 for longitudinal analyses. No significant difference between included and lost-to-follow-up patients was detected (Table S2). Results for the follow-up assessment after 1 year \((T1)\) are reported in Table 1. Patients underwent a significant increase in BMI, and SCL-90-R and EDE-Q scores significantly improved over the course of treatment (Table 1). An improvement in DERS scores was also observed, especially in the Goals and Impulse domains (Table 1).

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**Table 2** Goodness-of-fit measures for the initial model and all nested models

|          | \( \chi^2 \) | DF | CFI | TLI | RMSEA | SRMR | \( \Delta \chi^2 \) |
|----------|-------------|----|-----|-----|-------|------|-------------------|
| Initial model | 2.52       | 5  | 1.00 | 1.05 | 0.000 | 0.076 | –               |
| Trimmed models |           |    |     |     |       |      |                  |
| \( \alpha_{\text{EDE-Q}} = 0 \) | 11.70     | 6  | 0.94 | 0.90 | 0.089 | 0.104 | 9.18**          |
| \( \alpha_{\text{DERS}} = 0 \) | 8.78      | 6  | 0.97 | 0.95 | 0.062 | 0.116 | 6.26*           |
| \( \beta_{\text{EDE-Q}} = 0 \) | 27.35***  | 6  | 0.78 | 0.63 | 0.172 | 0.171 | 24.83***        |
| \( \gamma_{\text{EDE-Q}} = 0 \) | 17.97**   | 6  | 0.87 | 0.79 | 0.129 | 0.116 | 15.45***        |
| \( \varepsilon_{\text{EDE-Q}} = 0 \) | 13.83*    | 6  | 0.92 | 0.86 | 0.104 | 0.072 | 11.30***        |
| \( \zeta = 0 \) | 6.69      | 6  | 0.99 | 0.99 | 0.031 | 0.083 | 4.16*           |
| \( \theta = 0 \) | 38.55***  | 6  | 0.66 | 0.43 | 0.213 | 0.201 | 36.03***        |
| Unconstrained models |           |    |     |     |       |      |                  |
| \( \beta_{\text{DERS}} \neq 0 \) | 1.27      | 4  | 1.00 | 1.07 | 0.000 | 0.038 | 1.25            |
| \( \gamma_{\text{DERS}} \neq 0 \) | 2.51      | 4  | 1.00 | 1.04 | 0.000 | 0.081 | 0.02            |
| \( \varepsilon_{\text{DERS}} \neq 0 \) | 1.09      | 4  | 1.00 | 1.08 | 0.000 | 0.053 | 1.44            |
| \( \theta_{\text{EDE-Q}} \neq 0 \) | 2.45      | 4  | 1.00 | 1.04 | 0.000 | 0.077 | 0.07            |
| \( \eta_{\text{DERS}} \neq 0 \) | 1.59      | 4  | 1.00 | 1.06 | 0.000 | 0.048 | 0.93            |

Note: All comparisons were performed with the initial model as a comparator. *p < .05; **p < .01; ***p < .001.

Abbreviations: CFI, Comparative Fit Index; DERS, Difficulties in Emotion Regulation Scale; DF, degrees of freedom; EDE-Q, Eating Disorders Examination Questionnaire; RMSEA, Root Mean Square Error of Approximation; SRMR, Standardized Root Mean Square Residual; TLI, Tucker–Lewis Index.
The complex longitudinal relationship between EDE-Q and DERS scores was investigated using bivariate LCS analysis. The initial SEM model estimated LCs for both EDE-Q and DERS (ΔEDE-Q and ΔDERS, respectively), expressing the variations between baseline (EDET0 and DERST0) and follow-up (EDET1 and DERST1) measurements. The equations included constant change factors for both variables (αEDE-Q and αDERS coefficients, which were equivalent to the intercepts of LCs) and a proportional change factor for ΔEDE-Q, depending on EDET0 (βEDE-Q coefficient). The coupling between the two variables was initially set in a unidirectional way, by regressing ΔEDE-Q on both DERST0 (γEDE-Q coefficient) and ΔDERS (εEDE-Q coefficient). Finally, CTQ Total Score was entered in the model as a predictor of DERST0 (ζEDE-Q coefficient). The proportional change factor for DERS (βDERS coefficient), the effects of EDET0 and ΔEDE-Q on ΔDERS (γDERS and εDERS coefficients, respectively), and the effects of CTQ Total Score on both EDE-Q and DERS coefficients were initially constrained to zero; EDET0 and DERST0 were allowed to covary (ε coefficient). The complete equations for the proposed model are reported in Appendix S1.

This initial model showed excellent fit to the data, as indicated by the computed fit measures reported in Table 2. Using nested model comparisons, various trimmed models were tested in which all model coefficients were individually constrained to zero (Table 2). All constrained models were rejected, given that they showed worse fit measures, made less theoretical sense with respect to the a priori hypothesis, and yielded statistically significant difference tests, indicating a relevant loss in model fit (Table 2). Less restrictive unconstrained models were also tested by freeing previously constrained parameters. Despite having acceptable fit indices, these unconstrained models were also rejected since they did not significantly improve model fit (Table 2).

Figure 2 illustrates a diagram of the model, together with all estimated parameters. The fixed decrease in EDE-Q and DERS scores between T0 and T1 suggested by the mixed models reported in Table 1 was confirmed in the bivariate LCS, as indicated by statistically significant αEDE-Q and αDERS factors (Figure 2). In addition to this, a significant βEDE-Q effect was shown, indicating an improvement in ED-specific psychopathology that was proportional to the initial value (Figure 2), whereas no proportional change was observed for emotion dysregulation (Table 2). Regarding the longitudinal coupling between the two variables, a unidirectional effect of DERS scores on ΔEDE-Q was observed. In particular, baseline DERS scores predicted the EDE-Q trend over time (as shown by a significant γEDE-Q effect, Figure 2), indicating that patients who had higher levels of emotion dysregulation at the beginning of treatment achieved less ED symptom improvement. Moreover, EDE-Q latent change score was also significantly predicted by ΔDERS (εEDE-Q effect, Figure 2), suggesting that those who improved in emotional regulation during treatment improved more in ED-specific psychopathology. Conversely, neither the baseline EDE-Q scores nor its latent change score influenced the longitudinal trend of DERS, as demonstrated by the absence of a statistically significant increase in model fit upon the release of the relative regression coefficients (Table 2). The model was re-run with the addition of the possibility for ΔDERS to covariate with the

longitudinal variation of SCL-90-R GSI, in order to adjust for comorbid psychopathology; given that the model fit was slightly worse, and the rest of the model was essentially unchanged, this addition was not retained.

To conclude, the indirect effect of CTQ Total Score on ΔEDE-Q through the baseline DERS score was found to be statistically significant (ζEDE-Q = 0.12, 95% confidence interval [0.01, 0.31]), indicating that the presence of childhood traumatic experiences predicted reduced treatment efficacy for ED-specific psychopathology through the mediating effect of higher baseline DERS scores. Direct and total

FIGURE 2 Final bivariate latent change score model, illustrating the complex relationship between baseline scores and longitudinal variations following common path diagram conventions. Observed and latent variables are indicated with rectangles and circles, respectively, and single-headed arrows connecting them represent regression effects. Arrows departing from the triangle indicate intercepts, as triangles denote constants. Effects or variances that were constrained to zero are reported with grey arrows, whereas those constrained to one are shown using arrows with a “1.” Double-headed arrows represent variances and covariances. Unstandardized coefficients for all effects are reported above the corresponding arrows together with their labels, with standardized coefficients in parenthesis. The Greek symbol “Δ” denotes longitudinal variations. Arrows in bold indicate the proposed mediation paths. To facilitate model convergence, DERS and CTQ scores were divided by 10; estimated coefficients should be interpreted accordingly. p values are indicated as follows: *p < .05, **p < .01, ***p < .001. CTQ, Childhood Trauma Questionnaire; DERS, Difficulties in Emotion Regulation Scale; EDE-Q, Eating Disorders Examination Questionnaire.
effects were not significant (b = 0.03, p = .801 and b = 0.16, p = .272, respectively).

4 | DISCUSSION

This is the first study to investigate the complex relationship between childhood trauma, emotion dysregulation, and ED-specific psychopathology in patients with AN over the course of a multidisciplinary treatment including CBT-E. In accord with the main results of the study, both ED-specific psychopathology and emotion dysregulation improved after treatment. In addition, the amelioration of ED-specific symptoms showed both a constant and a proportional component with respect to the initial value, whereas only a constant longitudinal effect was observed for emotion dysregulation. Moreover, greater capacity for regulating emotions significantly predicted an improvement of EDE-Q scores, and not vice-versa.

The amelioration of ED-specific psychopathology at follow-up was an expected result considering that CBT-E is widely recognized as an efficacious treatment for AN (Dalle Grave et al., 2016; Fairburn et al., 2013; Fairburn, Cooper, & Shafran, 2003). The proportional effect according to which patients with higher levels of EDE-Q scores at baseline underwent a greater improvement had already been found in a previous study (Racine & Wildes, 2015). Indeed, patients with low ED-specific psychopathology levels at baseline were expected to benefit less from treatment, compared to those with higher initial EDE-Q levels who therefore showed more substantial decreases. This finding seems to indicate that the severity of core psychopathological features of the ED at baseline did not compromise the response to CBT-E. In other words, the present result pointed out that features other than the severity of ED-specific symptoms may play a role in determining whether a given patient will respond to CBT-E, and should be taken in consideration.

The results of this study seem to indicate that baseline emotion dysregulation predicted a worse 1-year outcome in terms of ED-specific psychopathology, which is consistent with previous observations (Haynos & Fruzzetti, 2011; Lavender et al., 2015; Treasure & Schmidt, 2013). Racine and Wildes (2015) found that higher emotion dysregulation predicted a worse outcome during the first year after the beginning of treatment, supporting the hypothesis that emotional dysregulation maintained the disorder and promoted relapses. Compared with previous observations, the present study was the first that considered baseline information in confirming the role of emotion dysregulation in the CBT-E outcome of patients with AN. Interestingly, a recent neuroimaging study observed that the neural correlates of altered emotion regulation in patients with AN significantly predicted a worse outcome in terms of weight restoration, giving further support to the results presented (Seidel et al., 2018).

The role of emotional dysregulation in the treatment outcomes for AN is in line with the affective model of pathological eating behaviors as dysfunctional coping strategies to manage adverse emotional states (Heatherton & Baumeister, 1991; Moulton et al., 2015; Overton, Selway, Strongman, & Houston, 2005). A possible explanation for the present results might be that even though CBT-E provides an integrative model for affective states (Fairburn, 2008), high levels of emotion dysregulation are not sufficiently challenged by this approach. This would contribute to maintaining pathological eating behaviors, as well as to the discontinuation of the treatment.

This mechanism has been also described in other mental disorders, where other types of behavior would assume the role of dysfunctional emotional regulation strategies (Sloan et al., 2017). This hypothesis is supported by preliminary evidence on the transdiagnostic efficacy of emotional regulation interventions in different psychiatric populations (Berking, Ebert, Cuijpers, & Hofmann, 2013; Sakiris & Berle, 2019; Sloan et al., 2017). It is also possible that motivation to change is affected by negative beliefs about emotions often associated with emotional dysregulation (Ford & Gross, 2019). For example, the belief that emotions are always uncontrollable shifts the locus of control outward, and this can compromise the outcome of psychotherapy by decreasing the patient's engagement (Delsignore & Schnyder, 2007).

Furthermore, the extended LCS bivariate model combined with mediation analysis made it possible to highlight that emotion dysregulation mediated the impact of childhood traumatic experiences in the determination of a worse prognosis. For the first time, the developed model of longitudinal outcome in AN seems to confirm the already postulated role of early trauma as a maintaining factor of ED-specific symptoms through emotion dysregulation (Racine & Wildes, 2014). Furthermore, the current result offers an explanation of the putative mechanisms through which childhood traumatic experiences are able to compromise treatment outcome in AN (Castellini et al., 2018; Castellini, Rossi, et al., 2020; Lelli et al., 2019). It should be noted that a significant indirect effect in the presence of a nonsignificant total effect may be a common occurrence in mediation analysis, and it does not undermine the presence and validity of the present findings (Agler & De Boeck, 2017; Rucker, Preacher, Tormala, & Petty, 2011).

The second noteworthy longitudinal effect was through the variation in DERS scores, meaning that patients who improved in emotion regulation also obtained greater benefits on ED-specific psychopathology. This result seems to confirm the importance of integrating the traditional EDs symptoms strategies of CBT with the emotion regulation modules of CBT-E (Dalle Grave et al., 2016; Fairburn et al., 2003). Indeed, it has been observed that a treatment solely focused on diet regulation and weight restoration did not lead to a parallel improvement in emotion dysregulation in a previous study (Haynos, Roberto, Martinez, Attia, & Fruzzetti, 2014).

Nevertheless, considering the 10% average reduction of DERS scores in patients, the observed improvement was not such as to reduce the levels of emotion dysregulation to levels observed in control participants. The present result could be partially explained in light of the ongoing debate on whether emotion dysregulation represents a trait or state condition in patients with AN (Harrison, Tchanturia, & Treasure, 2010). It is also possible that changes in emotion regulation could require longer follow-up observations.

The relationship between psychopathology and emotion regulation skills improvement was already observed in a previous study of patients with AN under an integrated CBT approach (Rowell,
MacDonald, & Carter, 2016); however, our study allowed overcoming the limitation of establishing a direction in this association. Indeed, the coupling effect is to be considered as unidirectional, since both paths were tested using SEM analysis, and that only the $\Delta$ERS$\rightarrow$ΔEDE-Q direction significantly improved model fit, whereas the opposite did not and was therefore rejected.

One of our study limitations is the relatively small sample size; therefore, our results should be considered as preliminary, and the proposed model be confirmed with a sample size better powered for SEM ($n = 200$ or more). Future studies with larger samples will also be able to enter the longitudinal variation of anxious-depressive symptoms in the model as a further LCS, to investigate their possible role. Moreover, the addition of more time-points will allow the examination of the impact of early trauma and emotion dysregulation on relapses after treatment. Finally, all psychopathological domains were only assessed using self-administered questionnaires.

Overall, these data reaffirm the importance of assessing emotion regulation skills over the course of psychotherapy-based multidisciplinary treatment of AN, and support the possible use of supplementary modules with a specific focus on this dimension, such as dialectical behavior therapy (Linehan, 1987), as already carried out in some ED treatment centers (Ben-Porath, Federici, Wisniewski, & Warren, 2014; Rowse et al., 2016). Finally, specific treatments for trauma-related psychopathology such as Eye Movement Desensitization and Reprocessing (Shapiro, 1989), cognitive processing therapy (Resick & Schnicke, 1992), or prolonged exposure therapy (Foa, 2011) could also be useful in selected cases of AN with early trauma, given the evidence pointing to their effectiveness in reducing emotion dysregulation (Galoski, Nixon, & Kayes, 2020; Puhalla, Flynn, & Vaught, 2021; Shapiro, 1989; van Toorenburg et al., 2020).

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CONFLICT OF INTERESTS
The authors declare that there are no conflict to interests.

DATA AVAILABILITY STATEMENT
The data underlying this article will be shared on reasonable request to the corresponding author.

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