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Boon, A.E.; Hauber, K.

Citation

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Note: To cite this publication please use the final published version (if applicable).
Cognitive emotion regulation strategies in relation to treatment outcome in a clinical sample of adolescents with personality disorders

Albert Eduard Boon1,2 | Kirsten Hauber2

1Parnassia Group: Youz, Child and Adolescent Psychiatry, The Hague, Netherlands
2Department of Child and Adolescent Psychiatry, Curium-Leiden University Medical Centre, Leiden, Netherlands

Correspondence
Albert Eduard Boon, Youz, Centre of Youth Mental Healthcare Haaglanden, Dr van Welylaan 2, 2566 ER, The Hague, The Netherlands.
Email: a.boon@parnassiagroep.nl

Abstract
The aim of this study was to examine cognitive emotion regulation strategies (CERS) of help-seeking adolescents diagnosed with personality disorders. At pre-treatment, patients (N = 116) were found to use some maladaptive but also some adaptive CERS more often than adolescents from the general population. Less than 4% of these pre-treatment CERS predicted treatment outcome. In patients whose treatment outcome according to the Symptom Checklist-90 (SCL-90) showed significant improvement (N = 75), a reduction of maladaptive CERS and an increase of adaptive CERS occurred. Patients that were unchanged or deteriorated (N = 41) showed no significant changes in CERS. In conclusion, pre-treatment CERS are not predictive for treatment outcome in this sample of adolescents diagnosed with personality disorders. Even though patients who use more adaptive and less maladaptive CERS have fewer symptoms, the relationship between these CERS and symptoms in this group of severe patients remains unclear.

KEYWORDS
adolescents, clinical, cognitive emotion regulation strategies, treatment outcome

1 | INTRODUCTION

Difficulties in applying emotion regulation (ER) skills are associated with symptoms of psychopathology and are common targets of treatment (Compas et al., 2017; Daros et al., 2021; Davies et al., 2011; Garnefski & Kraaij, 2018; Gross et al., 2019; Groth et al., 2019; Komescher et al., 2016; Potthoff et al., 2016; Rask et al., 2006). Nevertheless, research in this field is hard to compare because of the confusing number of different terms that are used to refer to emotion regulation-related processes. In a review on the status of research on ER, Gross (2015) states that there is considerable uncertainty as to what is meant by ER in many research reports. Therefore, Gross distinguishes between three ER processes in this field of research:

(a) coping: alleviating stress responses over a relatively long time,
(b) emotion regulation: which attempts to influence which emotions one has in certain situations and (c) mood regulation: which differs from emotion regulation because moods generally last longer than emotions (Gross, 2015; Gross & Thompson, 2007). To avoid negative or threatening emotions like anxiety, feeling threatened or depression, ER strategies seek to alter affect generation at the appraisal stage in which the individual valuates a situation as emotionally arousing.

In the process of dealing with potentially emotionally arousing stimuli, people are recurrently engaged in some form of emotion regulation. The strategies involved are (a) situation selection (choosing to avoid or approach an emotionally relevant situation), (b) situation modification (altering the physical environment), (c) attentional
deployment (directing one’s attention towards or away from an arousing situation) and (d) cognitive change (changing how to appraise a situation to alter its emotional meaning) (Gross, 1998). In the present research project, it is assumed that during psychotherapy in general, it is difficult to alter the external, physical environment (a), while (among other things) the therapist stimulates the patient to confront the emotionally relevant situation (b) and tries to direct the patient’s attention towards an emotional arousing situation (c). Hence, therapy encourages the patient to focus on her or his cognitive emotion regulation strategies (CERS) used to cope with emotionally arousing stimuli. Therefore, it is expected that during therapy patients learn about their preferred CERS and learn to better their cognitive skills.

Cognitive change or CERS refer to the conscious, cognitive way of handling emotionally arousing information (Thompson, 1991). In this ER strategies, cognitive skills (e.g., perspective-taking, challenging interpretations and reframing the meaning of situations) are used to modify the meaning of a situation or stimulus that gives rise to emotional reactivity. It can modify emotional reactions to stressful, anxiety-provoking situations and can lead to psychological flexibility and emotional well-being (Gross & Thompson, 2007). Maladaptive CERS are in general connected to various different forms of psychopathology (Caspi & Moffitt, 2018), and cognitive emotion dysregulation is considered a core feature of the problems of adolescents that cope with personality pathology (Compas et al., 2017; Gross, 2015; Schramm et al., 2013). Still much remains unclear about the CERS of help-seeking adolescents and to what extent different maladaptive and adaptive CERS are related to their treatment outcome.

In general, psychiatric patients appear to rely more on negative than on positive coping strategies, and pre-therapy coping strategies predict symptomatic outcomes in patients at risk for psychosis (Kommescher et al., 2016). Also, emotion regulation can be seen as a transdiagnostic treatment construct for patients with anxiety-, depression-, substance use-, eating- and borderline personality disorders (Sloan et al., 2017). Research on predictors of psychotherapy outcome among adults with anxiety and depressive symptoms suggest that higher levels of self-ignorance and self-blame at pre-treatment predict a poorer treatment outcome, while improvements in self-image is found to be a moderator for a favourable outcome in psychotherapy (Ryum et al., 2015).

The field of research on emotion regulation strategies that are common to adolescents who are treated for mental problems is fragmented, and the results are difficult to compare. The associations of coping and emotion regulation with symptoms of psychopathology may differ by gender depending on the developmental stage at which these constructs are measured, (Carlson & Grant, 2008; Schweizer et al., 2020; Sontag & Graber, 2010). In particular, adolescents’ developmental changes in emotion regulation depend on the maturation of affective control (Schweizer et al., 2020). In a meta-analysis on association between coping and emotion regulation and symptoms of psychopathology in childhood and adolescence, a small but significant positive association with symptoms was found for emotional suppression, avoidance and denial (Compas et al., 2017). A study on the relation between adolescents’ coping strategies and symptoms of depression and anxiety showed that rumination, self-blame, positive reappraisal and positive refocusing (the latter two inversely) were uniquely associated with depression symptoms, and catastrophizing and other-blame were uniquely related to anxiety symptoms (Garnefski & Kraaij, 2018).

The research about to what extent different maladaptive and adaptive coping strategies are predictive for and related to treatment outcome for adolescents is also fragmented and scarce. Coping strategies seem to be mechanisms of change to improve mental health outcomes in both clinical and non-clinical adolescents (Daros et al., 2021; Groth et al., 2019; Kendall et al., 2016; Sloan et al., 2017). In a meta-analysis of emotion regulation outcomes in psychological interventions for youth with depression and anxiety, it was found that psychotherapy decreases disengagement skills and increases engagement skills, which is correlated with a decrease in anxiety and mood symptoms (Daros et al., 2021). Studies with clinical samples show that pre-treatment coping behaviour contributes significantly to the prediction of post treatment symptom improvement in psychosis (Kommescher et al., 2016), eating disorders, psycho-physiological insomnia (van de Laar et al., 2015) and alcohol dependence (Rask et al., 2006). Although certain specific adaptive and maladaptive pre-therapy coping strategies were significantly associated with outcome in these studies, no clear predominance of either adaptive or maladaptive coping was found. In a study concerning post-traumatic stress disorder (PTSD), greater catastrophizing and less positive reappraisal pre-treatment showed significantly less reduction in PTSD hyperarousal symptoms (Davies et al., 2011). Only two (Davies et al., 2011; van de Laar et al., 2015) of the studies that focussed on the relation between pre-treatment CERS and treatment outcome used the same instrument (Cognitive Emotion Regulation Questionnaire) that was applied in the present study.

The most commonly used measures of emotion regulation (Gross et al., 2019) are the Emotion Regulation Checklist (Molina et al., 2014), Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004; Shields & Cicchetti, 1997), the Coping Flexibility Scale.
Kato, 2012) and the Cognitive Emotion Regulation Questionnaire (Compas et al., 2017; Garnefski et al., 2002). At the start of this research project (2008), the Cognitive Emotion Regulation Questionnaire (CERQ) was the preferred instrument because it had an adolescent version validated on adolescents in the general population, and the nine conceptually different cognitive emotion regulation strategies that are distinguished by the CERQ were found to be consistent across countries (Potthoff et al., 2016).

The aim of the present paper is a threefold exploration: first, to compare the pre-treatment cognitive emotion regulation strategies of adolescent patients (aged 14–22) with adolescents in the general population; second, to explore if and to what extent those strategies are predictive for therapy outcome according to a general factor of psychopathology; and, third, to examine the relationship between therapy outcome and changes in cognitive emotion regulation strategies.

2 | METHOD

2.1 | Sample

The participants were voluntary admissions to a partially residential psychotherapeutic facility of a youth psychiatry institution in the urban area of The Hague in The Netherlands. This facility offers a 5 days a week intensive mentalization-based treatment (MBT) (Bateman & Fonagy, 2006; Hauber, 2010) with partial hospitalization to adolescents with personality disorders between the ages of 16 and 23 years, although by exception a 14- or 15-year-old adolescent was accepted. Exclusion criteria are psychotic, autism spectrum and substance abuse disorders. Referrals come after prior outpatient treatment is proved to be insufficient. Motivation for treatment in both adolescent and system is a prerequisite for admission. The programme differs from the MBT programme offered for adolescents in England (Rossouw & Fonagy, 2012) using the psychodynamic group psychotherapy approach. The mentalizing focus of the various therapies is the adolescent’s subjective experience of himself or herself and others and on relationships with group members and staff. Weekly verbal and non-verbal group psychotherapies, such as group psychotherapy, art therapy and psychodrama therapy, are offered combined with individual and family psychotherapy. If necessary, medication is prescribed according to protocol by a psychiatrist on the staff. See Hauber et al. (2019) for more details and examples of the treatment programme.

At pre-treatment, 165 adolescents completed the questionnaires (T1), and 116 (70.3%) also completed the questionnaires at the end of treatment (T2). The group with complete measurements (T1 and T2) had a significantly longer duration of treatment (M 328.66 days, SD 133.45) than those with only T1 measurements (M 177.00 days, SD 138.14) (t = 6.76, p < .001). No differences were found for age, gender and personality disorders between those who completed both measurements and those who did not. Differences between these two groups were tested for all pre-treatment research variables (CERQ and SCL-90) and no significant results were found.

During this intensive MBT programme with average duration of 1 year with a maximum of 18 months, personality disorders, insecure attachment and symptoms may diminish (Hauber et al., 2017, 2018). The mean age at the start of treatment of this sample was 17.8 years (SD = 1.7, range = 14–22), and most (86.5%) of the group were female. The average duration of treatment was approximately 1 year (M = 337.2, SD = 138.9, range 90–693 days).

At pre-treatment, the borderline (37%), avoidant (51.9%) and depressive personality disorder (49.1%) according to the SCID-II were most common and in more than half of the cases in combination with one or more other personality disorders. All participants also had other clinically diagnosed comorbid non-psychotic disorders. All patients followed the treatment on a voluntary basis. Their level of education was average to above average. Dutch was spoken fluently by all participants.

2.2 | Instruments

The participating adolescents completed a set of web-based questionnaires at the beginning and end of treatment, including the CERQ (Garnefski et al., 2002), the SCL-90 (Arrindell & Ettema, 2003; Derogatis et al., 1973) and the Dutch Questionnaire for Personality Characteristics (Vragenlijst voor Kenmerken van de Persoonlijkheid [VKP]) (Duijnsen et al., 1996). Subjects were interviewed using the Structured Clinical Interview for DSM personality disorders (SCID-II) (Spitzer et al., 1990).

2.2.1 | VKP

The VKP is a questionnaire of 197 questions with answers with ‘true’ or ‘false’. The purpose of the VKP is to screen for personality disorders according to the DSM-IV. The VKP is recommended (Dingemans & Sno, 2004; Verheul et al., 2000) as a screening instrument for the Dutch version of the SCID-II. The outcome of the VKP indicates which SCID-II personality disorder sections should be used.

2.2.2 | SCID-II

The SCID-II is a structured interview of 134 questions. The purpose of this interview is to establish the 10 DSM-IV personality disorders and the depressive and the passive-aggressive personality disorder. The SCID-II corresponds with the DSM-IV (APA, 1994) in which the depressive and the passive-aggressive personality disorder are listed in Appendix B. The language and diagnostic coverage make the SCID-II most appropriate to be used with adults (age 18 or over) but with slight modification, it can be used with younger adolescents (Spitzer et al., 1990). Only the sections which were indicated by the outcome of the VKP were applied in the clinical interview.
Comparison of the cognitive emotion regulation strategies at pre-treatment with the general population

<table>
<thead>
<tr>
<th>Strategy</th>
<th>M</th>
<th>SD</th>
<th>t</th>
<th>p</th>
<th>ES (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-blame</td>
<td>65.6</td>
<td>9.9</td>
<td>16.99</td>
<td>&lt;.001</td>
<td>1.57</td>
</tr>
<tr>
<td>Acceptance</td>
<td>55.7</td>
<td>10.2</td>
<td>6.07</td>
<td>&lt;.001</td>
<td>0.57</td>
</tr>
<tr>
<td>Rumination</td>
<td>52.8</td>
<td>9.6</td>
<td>3.08</td>
<td>.003</td>
<td>0.28</td>
</tr>
<tr>
<td>Positive refocusing</td>
<td>45.0</td>
<td>11.7</td>
<td>-4.56</td>
<td>&lt;.001</td>
<td>0.46</td>
</tr>
<tr>
<td>Refocus on planning</td>
<td>48.3</td>
<td>8.9</td>
<td>-2.13</td>
<td>.035</td>
<td>0.19</td>
</tr>
<tr>
<td>Positive reappraisal</td>
<td>45.3</td>
<td>9.9</td>
<td>.87</td>
<td>.387</td>
<td>0.08</td>
</tr>
<tr>
<td>Putting into perspective</td>
<td>55.5</td>
<td>10.6</td>
<td>5.58</td>
<td>&lt;.001</td>
<td>0.53</td>
</tr>
<tr>
<td>Catastrophizing</td>
<td>49.3</td>
<td>9.6</td>
<td>-7.9</td>
<td>.431</td>
<td>0.07</td>
</tr>
<tr>
<td>Blaming others</td>
<td>49.9</td>
<td>9.1</td>
<td>-0.08</td>
<td>.935</td>
<td>0.01</td>
</tr>
</tbody>
</table>

a Small effect.
b Medium effect.
c Large effect.
3.2 | Relation between SCL-90 scores and coping strategies

The relation between the SCL-90 total score and the scales of the CERQ (Table 2) show that a higher level of psychopathology is positively related to the maladaptive scales self-blame and Rumination and negatively related to the adaptive scales positive refocusing and positive reappraisal. These relations are relatively stable during treatment. The correlation between the difference score (T2 – T1) of the SCL-90 are weak.

3.3 | Treatment duration

A comparison based on the number of personality disorders (0, 1 or more) showed no difference in treatment duration, F(2, 115) = 1.17, p = .32; also, no relation was found between treatment duration and SCL-score at the beginning of treatment (r = .084, p = .386) or scales of the CERQ (r = -.037 to .179, p > .05). The RCI-outcome groups were also not related to treatment duration, F(2, 115) = 1.53, p = .22.

3.4 | Pre-treatment variables as predictors for treatment outcome

The correlation between pre-treatment scores on the CERQ-scales and the SCL-90 outcome score are weak (Table 2). A regression analysis showed that less than 4% of the pre-treatment CERS predicted treatment outcome ($R^2 = .037, p = .212$) which was operationalized by differences in the total SCL-90 score. A model containing the CERQ-scales, gender, age at submission, treatment duration and pre-treatment SCL-90 score explained 12% of the variation ($R^2 = .121, p = .014$). This improvement can be attributed completely to the correlation between pre-treatment SCL-90 scores and the outcome score on the same instrument (r = .362, p < .001).

### TABLE 2 Correlations between of the cognitive emotion regulation strategies and the SCL-90 scores at pre- and post-treatment

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>SCL-difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>Self-blame</td>
<td>.504</td>
<td>&lt;.001</td>
<td>.611</td>
</tr>
<tr>
<td>Acceptance</td>
<td>.142</td>
<td>.130</td>
<td>.126</td>
</tr>
<tr>
<td>Rumination</td>
<td>.304</td>
<td>.001</td>
<td>.331</td>
</tr>
<tr>
<td>Positive refocusing</td>
<td>-.417</td>
<td>&lt;.001</td>
<td>-.455</td>
</tr>
<tr>
<td>Refocus on planning</td>
<td>-.174</td>
<td>.062</td>
<td>-.234</td>
</tr>
<tr>
<td>Positive reappraisal</td>
<td>-.357</td>
<td>&lt;.001</td>
<td>-.324</td>
</tr>
<tr>
<td>Putting into perspective</td>
<td>.067</td>
<td>.473</td>
<td>.186</td>
</tr>
<tr>
<td>Catastrophizing</td>
<td>.158</td>
<td>.089</td>
<td>.330</td>
</tr>
<tr>
<td>Blaming others</td>
<td>-.022</td>
<td>.813</td>
<td>.034</td>
</tr>
</tbody>
</table>

*Correlation between pre-treatment CERQ-scores and SCL-90 outcome.

3.5 | Relationship between changes in cognitive emotion regulation strategies and treatment outcome

When comparing the total SCL-90 pre-treatment versus post-treatment scores, a significant decrease was found (T1: M = 241.79, SD = 56.01; T2: M = 193.52, SD = 68.80; t = 8.58, p < .001, d = .77). Comparing pre- and post-treatment most of the cognitive emotion regulation strategies were found to show no or a small change, and some a medium change (Table 3). Changes in self-blame ($r = .433$), rumination ($r = .250$), positive refocusing ($r = -.385$), refocus on planning ($r = -.233$), positive reappraisal ($r = -.400$) and catastrophizing ($r = .260$) were significantly correlated with the SCL-90 difference score.

Reliable changed outcome groups were formed based on the SCL-90 scores. Patients that improved (N = 75) significantly (RCI) on the SCL-90 at post-treatment showed a large reduction effect on self-blame (p < .001, d = 1.15), a small reduction effect on rumination (p = .015, d = 0.36), a large increase effect on positive refocusing (p < .001, d = 0.88) and positive reappraisal (p < .001, d = 0.88), and a medium increase effect on refocus on planning (p < .001, d = 0.77). Patients that did not change (N = 25) or deteriorated (N = 16) did not show any significant changes in coping strategies.

4 | DISCUSSION

The aim of this study was to investigate the cognitive emotion regulation strategies (CERS) of a group of help-seeking adolescents diagnosed with personality disorders.

First, because cognitive emotion dysregulation is considered a core feature of the problems of adolescents diagnosed with personality pathology (Compas et al., 2017; Gross, 2015; Schramm et al., 2013), we compared the pre-treatment CERS of adolescent patients with adolescents in the general population. At pre-treatment adolescent patients were found to use not only the maladaptive CERS self-blame and rumination more often than non-clinical adolescents do, but also the adaptive CERS acceptance and putting into...
Cognitive emotion regulation strategies is in accordance with previous research with adults (Kommescher et al., 2016) and adolescents (Caspí & Moffitt, 2018; Compas et al., 2017). The finding that in our sample the adaptive strategies (acceptance and putting into perspective) were also used more often than in the norm population is not in agreement with past research findings.

Second, we explored if and to what extent those strategies were predictive for therapy outcome according to a general factor of psychopathology (SCL-90). In earlier studies with adults with anxiety and depressive symptoms (Ryum et al., 2015) it was found that the use of maladaptive strategies predicted less favourable treatment outcome. In our study however we conclude that pre-treatment CERS were not predictive for therapy outcome, because the predictability was found to be less than 4%. Of the other study variables only the pre-treatment symptomatology was a predictor for treatment outcome. This effect however must be attributed to fact that the same instrument was used as a predictor and as the outcome score and patients with a high initial score had a much larger chance at symptom reduction at the repeated measurement.

Third, we examined the relationship between therapy outcome and changes in cognitive emotion regulation strategies. It was assumed that reduction in psychopathology would be associated with change in CERS. It was found that the patients who improved significantly (N = 75) on the SCL-90 at post-treatment showed a reduction in the use of self-blame and rumination and an increase in positive refocusing, refocus on planning and positive reappraisal, while patients that did not change or deteriorated (N = 41) showed no significant changes in CERS. Therefore, it can be concluded that there is a relation between symptom reduction and changes in CERS, although the relationship between these strategies and symptoms remains unclear. Future research should focus on the causal relationship between symptom reduction and changes in CERS in clinical samples.

The results raise questions concerning the adaptiveness or maladaptiveness of the coping skill acceptance in combination with self-blame. The combination of an above average use of acceptance with a very high use of the maladaptive CERS self-blame at pre-treatment found in this research, makes one wonder if acceptance becomes a maladaptive CERS when it supports or even strengthens the use of self-blame. Especially in absence of the other adaptive CERS positive refocusing and putting into perspective. In addition, the role of the environment is important in relation to coping skills, as mental disorders are characterized by an inflexible and rigid pattern of responses to the environment (Aldao, 2013). One can imagine that for instance in the case of a patient who blames herself for the death of her little sister and also accepts this as the truth, she will be less likely to change this maladaptive CERS of self-blame concerning the loss of this family member. As in this example, this combination of self-blame and acceptance seems associated with inhibited aggression regulation problems. Presumably, a toxic combination evolves if not corrected by the environment which is related to a negative self-image. Prevention and treatment interventions should target this combination of CERS, in the context or the patient (Aldao, 2013). Moreover, this found combination of CERS is possibly illustrative of the clinical sample in this study with mainly girls with internalizing problems. Generalizability of these results is to be determined in other clinical samples.

In this study adaptive and maladaptive CERS are not predictive for therapy outcome. Possibly the severity of the psychopathology of this clinical sample influences the coping ability in general. In this way, the pre-treatment psychopathology severity is more indicative for treatment outcome (Davies et al., 2011; van de Laar et al., 2015) than the CERS. Nevertheless, based on the research so far on this topic, it is advised in (group) psychotherapy for clinical adolescents (a) to get an insight in the different adaptive and maladaptive CERS a patient uses to handle emotionally arousing situations, (b) to make the patient aware of her of his combination of CERS, (c) to explore the function of this combination of CERS in the context of the patient and (d) to find alternative coping strategies and practice new behaviour.

Limitations of this study should be mentioned. First, the sample of high risk adolescents examined in this study consisted of mainly girls with internalizing problems. Future research should also focus on other groups, for instance, adolescent boys with externalizing problems. Second, the comorbid disorders were not examined. Third, the potential heterogeneity of psychopathology captured by the SCL-90

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>t</th>
<th>p</th>
<th>ES (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-blame</td>
<td>14.22 4.31</td>
<td>11.20 4.18</td>
<td>6.78</td>
<td>&lt;.001</td>
<td>0.71*</td>
</tr>
<tr>
<td>Acceptance</td>
<td>12.52 3.88</td>
<td>13.38 3.29</td>
<td>-2.19</td>
<td>.030</td>
<td>0.21*</td>
</tr>
<tr>
<td>Ruminaton</td>
<td>11.10 3.84</td>
<td>10.40 3.40</td>
<td>1.79</td>
<td>.076</td>
<td>0.19</td>
</tr>
<tr>
<td>Positive refocusing</td>
<td>8.99 3.99</td>
<td>11.52 3.89</td>
<td>-6.44</td>
<td>&lt;.001</td>
<td>0.64*</td>
</tr>
<tr>
<td>Refocus on planning</td>
<td>10.94 3.42</td>
<td>12.73 3.48</td>
<td>-4.63</td>
<td>&lt;.001</td>
<td>0.52*</td>
</tr>
<tr>
<td>Positive reappraisal</td>
<td>9.23 3.80</td>
<td>11.41 4.05</td>
<td>-5.60</td>
<td>&lt;.001</td>
<td>0.56*</td>
</tr>
<tr>
<td>Putting into perspective</td>
<td>13.03 4.22</td>
<td>12.25 4.32</td>
<td>2.18</td>
<td>.031</td>
<td>0.18</td>
</tr>
<tr>
<td>Catastrophizing</td>
<td>6.46 2.62</td>
<td>6.04 2.22</td>
<td>-1.83</td>
<td>.070</td>
<td>0.17</td>
</tr>
<tr>
<td>Blaming others</td>
<td>6.25 2.52</td>
<td>6.65 2.44</td>
<td>-1.47</td>
<td>.145</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*Small effect.
**Medium effect.
was mentioned. Depending on which specific mental illnesses and comorbidities were present, the use of this measure to track ‘overall’ change might have a considerable amount of variance. Despite these limitations, this study is quite unique because little research has been done into personality disorders among adolescents (Courtney-Seidel et al., 2013; Hutsebaut et al., 2013; Sharp et al., 2016) and the relation of CERS and severe psychopathology among this group.

**CONFLICT OF INTEREST**

The authors declared no conflicts of interest.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author, (AEB), upon reasonable request.

**ORCID**

Albert Eduard Boon https://orcid.org/0000-0001-8667-6930
Kirsten Hauber https://orcid.org/0000-0001-5993-2820

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