CHAPTER 7

Understanding Emotion and Emotional Scarring in Recurrent Depression

Based on:
ABSTRACT

Background A single-item assessment of sad mood after remission from MDD is predictive of relapse, yet the mechanisms that play a role in depressive relapse remain poorly understood.

Methods In 283 patients, remitted from recurrent depression (DSM-IV-TR criteria; HDRS17 score ≤10), we examined emotional scarring, that is, whether the number of previous depressive episodes was associated with higher levels of sad mood as assessed with a Visual Analogue Mood Scale (VAMS). We then fitted a multivariate regression model to predict sad mood levels, including the Dysfunctional Attitude Scale Version-A, cognitive reactivity (Leiden Index of Depression Sensitivity), Ruminative Response Scale, and Everyday Problem Checklist.

Results Patients with greater numbers of prior episodes experienced higher levels of sad mood after remission. In multivariate regression, intensity of daily stress, number of previous MDEs, and dysfunctional beliefs were associated with the VAMS ($R^2 = .096$). Cognitive reactivity was not associated with sadness. After controlling for residual symptomatology, only the number of episodes remained significant.

Conclusions Our finding that patients with more previous MDEs reported higher levels of sad mood while remitted could be indicative of emotional scarring. Although dysfunctional beliefs and the intensity of daily stress were associated with sad mood, they did not predict sadness over and above residual symptoms. Thus, illness related characteristics especially are associated with sad mood after remission. More negative affect after remission could result in lower stress tolerance or more stress intensity could result in negative affect. Future studies should examine premorbid sadness in a longitudinal cohort, and should study the exact pathway from stress, affect, and cognition to relapse.
INTRODUCTION

Emotional states or affective experiences have been characterized as highly dynamic constructs (Golder & Macy, 2011; Gross & Muñoz, 1995; Watson & Clark, 1984). Within these dynamics, several authors have recently suggested some stability in the form of core affect (Barrett et al., 2005; Kuppens et al., 2010). The presence of negative affect itself, but also of affective inertia (the predictability of a current affective state by a previous state) has been related to the onset of affective disorders including Major Depressive Disorder (MDD) up to 2.5 years (for affective inertia; Kuppens et al., 2012) and 10 years later (for negative affect; Charles et al., 2013). Being one of the core symptoms of MDD (American Psychiatric Association, 2000), sad mood after remission is predictive of an early return of the disorder (Rucci et al., 2011; Van Rijsbergen et al., 2012). Besides being sad at one moment, reactivity of mood has also been found to predict relapse in depression (Lethbridge & Allen, 2008), even up to 5.5 years (Van Rijsbergen et al., 2013).

Although the number of previous MDEs is among the most consistent risk factors for relapse in depression (Bockting et al., 2006a; Hardeveld et al., 2013; Mueller & Leon, 1999), the influence of previous MDEs on sad mood levels after remission remains unexplored. Possibly, sad mood levels after remission are the result of emotional scarring due to a previous depressive episode. Whereas set point theory (Headey & Wearing, 1989) suggests that disturbances in affect are followed by return to baseline levels in the long run (i.e., the set point), more recent studies suggest that life events including unemployment, divorce, and widowhood lead to a new equilibrium instead (Lucas, Clark, Georgellis, & Diener, 2003; Lucas, Clark, Georgellis, & Diener, 2004). In one study, the affective set point was not yet reached up to eight years post-event (Lucas et al., 2003). These new set points potentially reflect an emotional scar as a result of prolonged exposure to stress or negative affect, similar to what occurs in MDD. Alternatively, patients with higher levels of sad mood before the onset of the first episode might have a poor prognosis for the course of depression.

Given the importance of monitoring sad mood after remission from MDD to detect relapse, we have recently focused on the assessment of sad mood using a Visual Analogue Mood Scale (VAMS). In these studies we demonstrated that a single-item VAMS was a predictor of time to relapse, with each centimeter increase resulting in increased risk of relapse by a factor 1.15 over a period of 5.5 years (Van Rijsbergen et al., 2012). Moreover, the VAMS had excellent diagnostic accuracy in the classification of a current depressive episode, both in terms of discriminative power and diagnostic accuracy (Van Rijsbergen et al., in press). Despite these promising results, it remains to be established whether sad mood deteriorates after experiencing a depressive episode (i.e., emotional scarring), and whether sadness is related to other well-known potentially modifiable vulnerability factors.
Relapse prevention interventions focus on potentially modifiable risk factors for relapse that are known to negatively influence the course of depression. These potentially modifiable risk factors include dysfunctional beliefs, cognitive reactivity, rumination and daily stress (Bockting et al., 2006a; Segal et al., 2006; Thase et al., 1992; for an overview see Beshai et al., 2011). Recent cognitive theories suggest that dysfunctional beliefs are mood state dependent (Lau, Haigh, Christensen, Segal, & Taube-Schiff, 2012; Roberts & Kassel, 1996; Zuroff, Blatt, Sanislow, Bondi, & Pilkonis, 1999), and their degree of activation by mild sadness caused by stressors signals vulnerability for depression (i.e., cognitive reactivity; Teasdale, 1988). However, the evidence for the mood state dependence of dysfunctional beliefs is highly mixed, since it was found that dysfunctional beliefs also predict relapse in depression without activation (Jarrett et al., 2012; Thase et al., 1992; Van Rijsbergen et al., 2013). Moreover, the experience of sadness or daily stress, without taking cognition into account, was found to predict relapse in depression directly (Bockting et al., 2006a; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000; Rucci et al., 2011; Van Rijsbergen et al., 2012). Therefore, it remains unclear whether belief activation (or the presence of dormant beliefs) is crucial in the causal chain from stress or negative affect to relapse in depression. Given that negative affect and the intensity and frequency of daily stress are related (Marco & Suls, 1993; Moberly & Watkins, 2008; Mor et al., 2010; Wichers et al., 2007), it could be that patients with higher sadness after remission experience more stressors or are more affected by daily stressors due to reduced stress tolerance. Alternatively, higher negative affect also could be the direct result of stressors (and all could be true).

The aim of the current study is to increase our understanding of the role of cognition, stress, and emotion in the pathway to depressive relapse. We will 1) examine whether patients with a higher number of previous MDEs experience higher levels of sad mood after remission, as suggested by the emotional scarring hypothesis; 2) study potentially modifiable correlates of sadness assessed after remission, including dysfunctional beliefs, cognitive reactivity, rumination, and the intensity and frequency of daily stress, whilst also including illness related variables (i.e., residual depressive symptoms, age of onset, number of previous depressive episodes, and last episode severity); and finally 3) attempt to replicate previous findings on the predictive validity of the VAMS by assessing whether baseline sadness (VAMS) predicts depressive symptomatology three months later.

**METHODS**

This study uses data from a research portal where patients with a remitted recurrent depression can participate in studies that specifically focus on the course and treatment of recurrent depression. The data from two randomized controlled trials, for readability referred to as Study A and Study B, were analyzed. Study A focused on Preventive Cognitive Therapy (PCT) in groups as an addition or alternative to Antidepressant Medication (ADM)
versus ADM alone in the prevention of relapse in recurrent depression (Bockting et al., 2011a). Study B examined the effectiveness of an internet adaptation of PCT added to Treatment-As-Usual (TAU) versus TAU alone in the prevention of relapse in recurrent depression (Bockting et al., 2011b). Both protocols were approved by the Medical Ethical Committee for Mental Health Institutions and all patients provided written informed consent prior to participation.

**PARTICIPANTS**
In both studies, patients were included who had a) experienced at least two lifetime Major Depressive Episodes (MDEs), of which the last MDE was no longer than two years ago; b) current remission of the last MDE for at least two months, both defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV) and assessed with the Structured Clinical Interview for DSM–IV Disorders (SCID-I; First et al., 1995) administered by trained psychologists and researchers; and c) a current score of $\leq 10$ on the 17-item Hamilton Depression Rating Scale (HDRS$_{17}$). Exclusion criteria were: current mania, hypomania, a history of bipolar illness, any psychotic disorder (current and previous), organic brain damage, current alcohol or drug abuse, predominant anxiety disorder, and recent electroconvulsive therapy. Both studies included remitted patients, but differed to the extent that Study A only included patients who a) were currently on ADM for at least six months, and b) did not receive psychotherapy more frequent than twice per month. In Study B, there were no restrictions with respect to both type and frequency of current care (i.e., psychotherapy, ADM, specialty care, no care).

**MEASURES**

*Relapse in MDD*
SCID-I interviewers attended regular consensus meetings to enhance inter-rater agreement. Potential relapses during follow-up were assessed for all patients using the SCID-I at four assessment points in Study A: $T_2$ (after 3 months), $T_4$ (after 9 months), $T_6$ (after 15 months), and $T_7$ (after 24 months), and at three assessment points in Study B: $T_2$ (after 3 months), $T_5$ (after 12 months), and $T_9$ (after 24 months). Intermittent assessment points did not include an interview or VAMS, and are therefore not presented.

*Visual Analogue Mood Scale (VAMS)*
Patients were asked to rate their current mood on a telephone-assisted version of a Visual Analogue Mood Scale (VAMS) previously used in mood induction procedures (Segal et al., 1999; Van Rijsbergen et al., 2013). By telephone, patients received the following instruction: ‘Please rate your current mood on a scale of 0 to 100, on which 0 indicates ‘happy’, and 100 indicates ‘sad’ and their answer was noted by the interviewer.
Inventory of Depressive Symptomatology – Self Report (IDS-SR)

The Dutch translation of the 30-item IDS-SR (Rush et al., 1996) was used to assess levels of depressive symptomatology. The IDS-SR is a self-report measure on which patients rate their symptoms on a scale of zero to three. The IDS-SR rates all DSM-IV core symptom domains including mood, cognitive and psychomotor symptoms, but also commonly associated symptoms including anxiety. The IDS-SR has excellent internal consistency ($\alpha = .92$; Rush et al., 2003).

Everyday Problem Checklist (EPCL)

We used the Dutch translation of the Everyday Problem Checklist to assess the occurrence of 114 daily stressors in the three months preceding the measurement point. Based on the manual (Vingerhoets & Van Tilburg, 1994), we created two scores: the frequency and the intensity of daily stress. The frequency of daily stress was the sum of all items that were experienced, and ranged from 0 to 114. The intensity of daily stress reflects the impact of stressors and was calculated by dividing the total intensity of all items by the frequency, resulting in a score with a range of 0 (‘no impact’) to 3 (‘major impact’). In the current study, the reliability across all items was excellent ($\alpha = .92$).

Dysfunctional Attitude Scale – Version A (DAS-A)

In the current study the Dutch adaptation (Douma, 1991) of the DAS-A (Weissman, 1979) was used to assess dysfunctional beliefs. On the DAS-A patients rated their agreement with all 40-items on a seven-point scale that ranged from ‘totally agree’ to ‘totally disagree’. The DAS-A demonstrated excellent reliability in a previous study ($\alpha = .86$; Dozois et al., 2003), and had a reliability of $\alpha = .95$ in the current study.

Leiden Index of Depression Sensitivity (LEIDS)

The LEIDS is a self-report questionnaire that aims to measure cognitive reactivity to sad mood independent of mood induction (Van der Does, 2002). After imagining a mildly depressed mood, patients rated all 34-items on a scale that ranged from one ‘not applicable’ to five ‘strongly applicable’. An exemplary item is ‘When I feel sad, I feel I can afford fewer mistakes’. The LEIDS was found to be significantly associated ($r = .43$) with changes in dysfunctional beliefs following mood induction (Van der Does, 2002). Cronbach’s alpha in the current study was .90.

Ruminative Response Scale (RRS)

Rumination was assessed using the validated Dutch adaptation of the RRS, the RRS-NL (Raes & Hermans, 2007). Patients rated their agreement on a scale that ranged from ‘almost always’ to ‘almost never’. The five-item subscale brooding was used, as this aspect of rumination appears to specifically reflect dysfunctional and maladaptive thinking and is related to depression later in time (Treynor et al., 2003). In the current study, Cronbach’s alpha for the total RRS was .91, and .74 for the brooding subscale.
**Personality Diagnostic Questionnaire 4+ (PDQ-4+)**

The PDQ-4+ (Hyler, 1994) is a self-report personality questionnaire with 99 true/false items that directly correspond to personality disorders in the DSM-IV. For the current study we used the total PDQ-4+ score, which reflects overall continuous levels of personality pathology. The psychometric properties of the PDQ-4+ appear to be reasonable, with adequate internal consistency in a recent study (Cronbach’s alpha between .49 and .75; Hopwood et al., 2012). Lower internal consistencies of the PDQ-4+ have also been attributed to the nature of PDs (Carr & Francis, 2010; McHoskey, 2001). Cronbach’s alpha for the total overall dimensional score was .92 in the current study.

**PROCEDURE**

The procedure for both studies was similar. Upon entry in the studies, patients were followed for two years. During the baseline and follow-up telephone interviews, the VAMS was administered first, followed by the SCID-I and then the HDRS, interview. In the same week, the IDS-SR, DAS, LEIDS, RRS, and EPCL were administered online, which patients could access through a personalized hyperlink. These measures were administered at all assessment points, except for T_4 and T_7 in Study A. Both T_4 and T_7 from Study A were therefore not included in the current manuscript. The PDQ-4+ was administered at baseline in both studies (T_0). Patient recruitment for the respective studies started in 2009 (Study A) and 2010 (Study B), with the VAMS being administered before every SCID-I interview since March 2012. This implies that, depending on the moment of inclusion, the time from inclusion up to the assessment of the first VAMS differed between patients and could be zero (first VAMS at inclusion for patients included after March 2012) up to 24 months (first VAMS at final assessment point).

**DATA ANALYSIS**

After inspection of VAMS scores we found that the VAMS showed a modest deviation from the normal distribution. Therefore the VAMS scores were square root transformed, which improved normality. For reasons of clarity and interpretation, descriptives reflect untransformed data. In total 9.8% of data were missing, presumably at random. Multiple imputation was used to account for missing data. Following suggestions from Bodner (2008), we used 12 imputations to account for missing data.

First, we examined evidence for the presence of emotional scarring in recurrent depression. We therefore correlated the number of previous MDEs with the VAMS score. A post-hoc median split was used to divide the sample according to the median in ≤ 4 versus > 4 previous MDEs, followed by ANOVA to assess differences in sadness based on the median split. Fitting our research question, the data comprised of the first assessment point for each patient including a VAMS. First complete assessment points were collapsed across patients and do therefore not represent a specific time point.
Second, we examined potentially modifiable and illness-related correlates of higher levels of sadness after remission and aimed to fit the most optimal multivariate regression model. Variables for the multivariate model were selected using univariate regression with the VAMS as the dependent variable. Variables that were associated with the VAMS with $p < .10$ were retained and were subsequently entered in a multivariate regression model with the VAMS as the dependent variable. We analyzed a multivariate model with and without illness related variables (i.e., age of onset, number of previous MDEs, and last MDE severity). Since we had no a-priori reasons to include one predictor in the model before the other, we used backward stepwise linear regression. After entering all independent variables, the variable with the smallest $t$ statistic was removed (provided that $p > .10$). This process was repeated until no variables were removed. We used continuous levels of personality pathology (PDQ-4+) to assess whether personality pathology confounded the results. As backward stepwise regression is not compatible with a dataset including several imputations, the non-imputed original dataset was used ($n = 202$). For this analysis, 13 patients who had relapsed at the time the VAMS was assessed were excluded because we were interested in correlates of sad mood after remission.

Finally, we attempted to replicate previous findings concerning the predictive validity of the VAMS in an independent dataset. To prevent any intervention effects, only patients in the control groups from both studies (AD alone in Study A, TAU alone in Study B) were selected, resulting in a subsample of 67 patients who filled out the VAMS at $T_0$. As we were interested in the course of depressive symptomatology, patients with a relapse at $T_2$ were not excluded (and all patients were remitted at $T_0$). We used linear regression analysis with the VAMS$_{T_0}$ as the independent variable and the IDS-SR$_{T_2}$ as the dependent variable with and without controlling for $T_0$ depressive symptomatology (ISD-SR).

RESULTS

PRELIMINARY ANALYSES

Before combining the datasets from both studies, we first examined potential differences between both studies. Patients of Study A did not differ meaningfully from those of Study B on the most important outcome measures: VAMS scores and depressive symptomatology (all $p s > .05$). Concerning clinical characteristics both samples differed with respect to dysfunctional beliefs, which were higher in Study B ($M_{Study\ A} = 118.65, SD = 28.21; M_{Study\ B} = 130.37, SD = 35.16; F(1, 226) = 5.42, p = .021$), and the frequency of daily hassles, which were also higher in Study B ($M_{Study\ A} = 30.52, SD = 13.61; M_{Study\ B} = 36.97, SD = 16.48; F(1, 215) = 7.13, p = .008$). After dichotomizing the number of previous MDEs in two versus more, three versus more, four versus more, and five versus more MDEs, a difference emerged in that there were significantly fewer patients with two MDEs in Study A than in Study B (12% in Study A, 24% in Study B; $\chi^2(1, N = 283) = 4.22, p = .04$). Moreover, as expected from
differences in inclusion criteria, ADM use at inclusion was significantly higher in Study A than in Study B (Study A: 100%, Study B: 51%; $\chi^2 (1, N = 283) = 51.78, p < .001$). Possibly as a reflection of this, patients in Study A also more often had a severe (compared to mild) previous MDE than in Study B (70% severe compared to mild in Study A, 50% severe compared to mild in Study B; $\chi^2 (1, N = 134) = 4.09, p = .043$).

As there are some indications that ADM use might affect patients’ emotional experiences (Price et al., 2009), we also examined whether patients with versus without ADM use differed on the included clinical measures (dysfunctional beliefs, cognitive reactivity, brooding, intensity/frequency of daily stress, continuous personality pathology, VAMS, IDS-SR, inclusion HDRS), which was not the case for any of the measures (all $p$s > .05). Since the trials were highly similar on the most important measures, we subsequently merged the data.

**PATIENTS**

The demographic and clinical characteristics of all patients ($N = 283$) are depicted in Table 7.1. Most patients were female (72.4 %) and were remitted ($M_{HDRS_{17}} = 3.24, SD = 2.86$) from a median of 4 previous depressive episodes (IQR = 2.0). More than 75% of all patients had a moderate or severe previous MDE.
Table 7.1: Patient demographic and clinical characteristics (N = 283)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Descriptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>283</td>
<td>72.4</td>
</tr>
<tr>
<td>Age</td>
<td>283</td>
<td>47.1 (10.6)</td>
</tr>
<tr>
<td>Married or cohabiting (%)</td>
<td>279</td>
<td>65.6</td>
</tr>
<tr>
<td>Patients on antidepressants (%)</td>
<td>283</td>
<td>62.9</td>
</tr>
<tr>
<td>Current psychotherapy (%)</td>
<td>262</td>
<td>26.3</td>
</tr>
<tr>
<td>Median previous MDEs (IQR)</td>
<td>283</td>
<td>4.0 (2.0)</td>
</tr>
<tr>
<td>Age of first onset</td>
<td>279</td>
<td>28.6 (12.4)</td>
</tr>
<tr>
<td>Severity last MDE a</td>
<td>283</td>
<td>21.5</td>
</tr>
<tr>
<td>Mild (%)</td>
<td></td>
<td>52.7</td>
</tr>
<tr>
<td>Moderate (%)</td>
<td></td>
<td>25.8</td>
</tr>
<tr>
<td>Severe (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total inclusion HDRS17</td>
<td>283</td>
<td>3.2 (2.9)</td>
</tr>
<tr>
<td>Visual Analogue Mood Scale (VAMS)</td>
<td>277</td>
<td>30.2 (22.3)</td>
</tr>
<tr>
<td>Depressive symptomatology (IDS-SR)</td>
<td>235</td>
<td>16.3 (10.4)</td>
</tr>
<tr>
<td>Frequency of daily hassles (EPCL)</td>
<td>217</td>
<td>35.3 (16.0)</td>
</tr>
<tr>
<td>Intensity of daily hassles (EPCL)</td>
<td>217</td>
<td>1.2 (0.5)</td>
</tr>
<tr>
<td>Dysfunctional attitudes (DAS)</td>
<td>228</td>
<td>127.3 (33.8)</td>
</tr>
<tr>
<td>Cognitive reactivity (LEIDS)</td>
<td>223</td>
<td>101.4 (17.6)</td>
</tr>
<tr>
<td>Brooding (RRS)</td>
<td>219</td>
<td>11.0 (3.1)</td>
</tr>
<tr>
<td>Continuous personality score (PDQ-4+)</td>
<td>281</td>
<td>23.3 (12.1)</td>
</tr>
</tbody>
</table>

Note. Descriptive characteristics represent mean (SD) unless stated otherwise. MDE = Major Depressive Episode, IQR = Interquartile range, HDRS17 = 17-item Hamilton Depression Rating Scale, PD = Personality Disorder.

a Last MDE severity is based on the number of SCID-I depression symptoms (5 symptoms corresponds to mild, 6-7 symptoms corresponds to moderate, whereas 8-9 symptoms corresponds to severe depression).

EMOTIONAL SCARRING IN RECURRENT DEPRESSION

We first examined whether we could find an association between the VAMS and the number of previous MDEs, which could be indicative of emotional scarring. First, there was a modest, but significant, positive association between the number of previous MDEs and the VAMS score ($r_s = .15, p < .018$). Following a post-hoc median-split, we found that remitted patients with more than four previous MDEs scored significantly higher on the VAMS ($M_{>4} = 33.39, SD = 22.87$) than remitted patients with four or fewer previous MDEs ($M_{\leq4} = 25.62, SD = 19.39; F(1, 268) = 5.36, p < .025$).

ASSOCIATIONS BETWEEN VULNERABILITY FACTORS OF RELAPSE AND SADNESS

In univariate regressions, the following potentially modifiable and illness-related variables were related to the VAMS at $p < .10$: dysfunctional beliefs ($\beta = .23, t(211) = 3.41, p = .001$, adjusted $R^2 = .05$), cognitive reactivity ($\beta = .13, t(207) = 1.89, p = .06$, adjusted $R^2 = .01$), perceived intensity of daily stress ($\beta = .25, t(203) = 3.63, p < .001$, adjusted $R^2 = .06$), and finally, the number of previous MDEs ($\beta = .13, t(262) = 2.05, p = .04$, adjusted $R^2 = .01$).
These variables were subsequently entered in a backward stepwise regression with the baseline VAMS as the dependent variable. In the first step dysfunctional beliefs, cognitive reactivity, the intensity of daily stress, and the number of previous MDEs were included. A second model without the number of previous MDEs was highly similar; therefore the results are not reported. The final prediction model including both potentially modifiable vulnerabilities as well as the number of previous MDEs contained three predictors and was reached in two steps. The overall model was statistically significant \( F(3, 201) = 7.08, p < .001 \), and was able to account for 9.6% of the variance in the VAMS score \( R^2 = .096, \text{Adj. } R^2 = .082 \). Higher VAMS levels after remission were associated with higher levels of dysfunctional beliefs, a higher perceived intensity of daily stress, and a higher number of previous MDEs (Table 7.2). The perceived intensity of daily stress received the strongest weight in the regression model \( (\beta = .19) \), followed by both dysfunctional belief levels \( (\beta = .14) \), and the number of previous MDEs \( (\beta = .14) \). Personality pathology did not confound any of the predictors, and the associations of dysfunctional beliefs and the intensity of daily stress did not depend on the number of previous MDEs (i.e., interaction effects not significant). However, after controlling for levels of depressive symptomatology with the IDS-SR, only the number of previous MDEs remained significant in the model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>( B )</th>
<th>SE ( (B) )</th>
<th>( t )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>2.02</td>
<td>.68</td>
<td>2.98</td>
<td>.003</td>
</tr>
<tr>
<td>Intensity of daily stress</td>
<td>.90</td>
<td>.36</td>
<td>2.52</td>
<td>.012</td>
</tr>
<tr>
<td>Dysfunctional beliefs</td>
<td>.01</td>
<td>.01</td>
<td>1.89</td>
<td>.060</td>
</tr>
<tr>
<td>Number of previous MDEs</td>
<td>.13</td>
<td>.06</td>
<td>2.09</td>
<td>.038</td>
</tr>
</tbody>
</table>

Note: The VAMS is square-root transformed. VAMS = Visual Analogue Mood Scale

**Table 7.2:** Final backward multivariate regression model \( (n = 201) \) with VAMS levels after remission as dependent variable

**REPLICATION OF THE PREDICTIVE VALIDITY OF THE VAMS**

Finally, we examined whether we could replicate the predictive validity of the VAMS as has been demonstrated in a previous study (Van Rijsbergen et al., 2012). We were able to replicate our previous findings since the baseline VAMS was a significant predictor of depressive symptomatology three months later \( (B = 1.83, \text{SE} = .77, p = .02, \text{semi-partial } r = .32, \text{FMI} = .25) \), see Table 7.3. After controlling for baseline depressive symptomatology, the extent of prediction by the VAMS decreased, but still evidenced a nonsignificant trend \( (p = .08) \).
### DISCUSSION

In the current study, we attempted to increase our understanding of emotions and emotional scarring in recurrent MDD. First, we found that patients with a greater number of previous depressive MDEs reported higher levels of sad mood after remission. The mean difference of 7.8 points on the VAMS between patients with ≤4 and >4 episodes appears to be clinically relevant, as we previously found that every one-point increment on the VAMS increased risk of relapse by a factor 1.15 (Van Rijsbergen et al., 2012). This finding implies that scarring by previous episodes could have occurred. Alternatively, our findings could also be explained by higher levels of sadness before the very first episode onset in our sample, which increased the risk for developing a higher number of depressive episodes.

In contrast with the scarring hypothesis, a previous study demonstrated in adolescent girls that premorbid negative emotionality (i.e., temperamental emotional arousal and intensity) increased with the onset of MDD, but returned to premorbid levels again after remission of the MDE (Beevers, Rohde, Stice, & Nolen-Hoeksema, 2007).

We found two potentially modifiable variables and one illness related characteristic that were significantly associated with relatively higher levels of sad mood in a multivariate model: higher perceived intensity of daily stress, higher levels of dysfunctional beliefs, and a greater number of previous MDEs. However, after controlling for depressive symptomatology, only the number of previous MDEs (and not the potentially modifiable variables) was associated with sad mood. Our findings could imply that, after remission, the influence of daily stress and dysfunctional beliefs on sad mood are largely an epiphenomenon of MDD. However, given that we only have cross-sectional data and found that levels of sad mood appear to be influenced by the number of previous MDEs, we cannot rule out that sad mood itself might be a consequence of the disorder. Still, we were able to replicate that sad mood levels predicted depressive symptomatology three months later at a trend-level after correction for current levels of depressive symptomatology. Surprisingly, and not in line with recent cognitive models (Teasdale, 1988), cognitive
reactivity was not associated with sad mood below the conventional .05 alpha level, and was not included in the multivariate model. Patients with higher levels of sad mood after remission did not report more frequent stressors, but instead appeared to be affected more by the stressors they encountered. Preventive interventions might reduce negative affect through modifying the impact of daily stress, which has already been demonstrated indirectly (Bockting et al., 2006b). Alternatively, preventive interventions also might alter affective experiences themselves (Batink et al., 2013). Future studies should examine the pathway from stressors to negative affect to depressive relapse or whether negative affect might result in intolerance of subsequent stressors.

The potentially modifiable variables that we examined in relation to sad mood could determine levels of positive affect as well. Positive affect appears to be important in depression since it was found that patients with a current episode of recurrent MDD who responded with a drop of negative affect in response to increases in positive affect during the course of the day had a better prognosis, and responded better to treatment (Wichers, Lothmann, Simons, Nicolson, & Peeters, 2012). In the current study we did not include several variables (life-events, coping, and emotion regulation) that might be related to sad mood, including genetic factors, which were able to explain 18% of variance in momentary negative affect in a previous study (Jacobs et al., 2013).

Strengths of our study include our large sample of remitted patients hence limiting mood state effects of depression, and the use of well validated questionnaires and interviews. Several limitations of the current study have to be taken into account. First, we combined patients from two different RCTs. Although this increased our sample size and patients were very similar on most characteristics, they did differ with respect to the number of previous MDEs, previous MDE severity, and dysfunctional belief levels which might have influenced the strength of the associations we found. Second, personality pathology was only assessed at baseline (T_0). Patients’ initial levels of personality pathology might no longer reflect personality pathology 3-24 months later, which might explain the absence of association with the VAMS. However, this does not appear to be very likely, since personality pathology is relatively stable, with fluctuations being inherent to the disorder itself (Lopez-Castroman et al., 2012; Morey et al., 2010). Third, cognitive reactivity was assessed using a self-report questionnaire and not by a mood-induction procedure. Finally, due to the nature of our design, we are not able to examine whether the potentially modifiable correlates of the VAMS are in fact determinants of sadness or concomitants.

In sum, we found that patients with a greater number of previous depressive MDEs reported higher levels of sadness, which could be indicative of emotional scarring. Moreover, three variables were associated to sadness after remission: the intensity of daily stress, level of dysfunctional beliefs, and the number of previous MDEs. However, after controlling for depressive symptomatology only number of previous MDEs (an illness related characteristic) appeared to be associated to sad mood after remission. This finding
calls into question the role of cognitive factors as determinants for sad mood, although cognitive factors might determine positive affect. Remarkably, and also not in line with recent cognitive models (Teasdale, 1988), cognitive reactivity was not related to higher levels of sadness. We found no indication that patients with higher levels of sad mood reported more stressors. Future studies should attempt to more closely examine the causal sequence of these variables to both positive affect, negative affect, and relapse in depression using experience sampling methods.