Ambulatory emotional reactivity to negative daily life events predicts remission from major depressive disorder

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ABSTRACT

Major depressive disorder (MDD) is often associated with altered emotional reactivity. However, the functional significance of altered emotional reactivity in MDD is uncertain. This study was the first to examine the predictive relationship between intensely sampled ambulatory emotional reactivity and the clinical course of MDD. Forty-six outpatients who met criteria for MDD underwent six days of experience sampling of their ambulatory reactivity to everyday negative and positive life events. After experience sampling, all outpatients received pharmacotherapy with supportive psychotherapy and were followed clinically for 18 months. At one month, less emotional reactivity to negative and positive daily events predicted higher depressive symptom severity. Importantly, patients who exhibited less negative emotional reactivity to daily negative life events were less likely to recover from MDD over the 18 month follow-up. Relationships between ambulatory emotional reactivity and MDD course were not accounted for by the duration or the severity of initial MDD symptoms. Diminished ambulatory emotional reactivity appears to be functionally significant in depression. Intensive sampling of ambulatory emotions may have utility for predicting the clinical course of MDD.

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Major depressive disorder (MDD) is classified among the mood disorders by the Diagnostic and Statistical Manual (DSM-IV) and is defined by persistent mood disturbance involving elevated sadness and/or loss of pleasure and interest in daily activities (APA, 2000a). Researchers have increasingly described how MDD alters short-term emotional reactivity to environmental stimuli (e.g., Davidson, Pizzagalli, Nitschke, & Putnam, 2002). Three competing views of how MDD alters reactivity to emotional stimuli have emerged: positive attenuation (reduced reactivity to positive stimuli), negative potentiation (increased reactivity to negative stimuli), and emotion context insensitivity (ECI; reduced reactivity to both positive and negative stimuli). Although most work examining these views is cross-sectional (see Bylsma, Morris, & Rottenberg, 2008, for a review), each view postulates one or more core affective deficits in MDD that presumably interfere with normal daily functioning and influence long-term MDD course. We briefly review relevant theory and findings related to this question.

Investigations into the factor structure of emotional experience converge on two-factor models, often labeled positive affect (PA) and negative affect (NA) (Watson & Tellegen, 1985). Related theoretical perspectives highlight the functional significance of PA and NA, connecting these factors to broader affective systems governing approach and withdrawal motivation, respectively (Depue & Collins, 1999; Gray, 1973; Watson, Wiese, Vaidya, & Tellegen, 1999). The PA system is associated with behavioral approach and is characterized by feelings such as enthusiasm, interest, and satisfaction. The NA system is associated with behavioral withdrawal and is characterized by feelings such as anxiety, nervousness, and guilt (Watson et al., 1999). In sum, functionalist models of affect view PA and NA reactions as generally facilitating adjustment to environmental opportunities and threats (e.g., Levenson, 1999). Consistent with this premise, a growing body of research demonstrates that PA and NA can predict the development and outcome of MDD (Morris, Bylsma, & Rottenberg, 2009; Wichers et al., 2007, 2009). Extending this body of work, it can be expected that also reactivity of NA and PA will be salient to MDD course.

Importantly, the three major views of emotion in MDD make more specific predictions about the relationships between emotional responses and MDD course. The positive attenuation view of MDD characterizes its core affective pathology in terms of reduced responsiveness to appetitive stimuli and/or a reduced drive to engage with positive or rewarding environmental...
situations (Henriques & Davidson, 2000). Cross-sectional studies consistently support this view (Bylsma et al., 2008). Within the functional framework described earlier, the positive attenuation view predicts that those depressed individuals with the lowest PA reactivity to positive stimuli will have the worst MDD course. This view has some support in prospective studies. One experiment found blunted emotional responses to an amusing film predicted MDD non-recovery (Rottenberg, Gross, Wilhelm, Najmi, & Gotlib, 2002). More recently, decreased PA reactivity after negative mood induction in remitted depressed patients predicted relapse during follow-up (Lethbridge & Allen, 2008). Weaker evidence, such as studies that relied on trait-measures of PA reactivity (e.g., Behavioral Activation Scale; Carver & White, 1994) or self-reported anhedonia have found a more chronic MDD course (Kasch, Rottenberg, Arnow, & Gotlib, 2002; McFarland, Shankman, Tenke, Bruder, & Klein, 2006; Spijker, Bijl, de Graaf, & Nolen, 2001; for an exception, see Clark, Fawcett, Salazar-Grueso, & Fawcett, 1984).

The negative potentiation view of MDD characterizes its core affective pathology largely in terms of exaggerated NA reactivity. Despite the fact that the negative potentiation view has spawned a powerful therapy for depression (cognitive behavior therapy; CBT), only limited cross-sectional support for the negative potentiation hypothesis exists with numerous non-supportive results (Bylsma et al., 2008). The negative attenuation view predicts that those depressed individuals with the greatest NA reactivity to negative stimuli will have the worst MDD course. Studies show equivocal results. Consistent with this view, it has been shown that patients with the smallest emotional responses to stress in their daily lives had a more favorable course during therapy with CBT (Cohen et al., 2008; Gunthert, Cohen, Butler, & Beck, 2005). Furthermore, NA responses to daily events decreased during BCT but, somewhat contrary to prediction, NA reactivity to negative thoughts increased during CBT (Parrish et al., 2009). By contrast, blunted autonomic reactivity to a sad stimulus has been shown to predict a worse MDD course (Rottenberg, Salomon, Gross, & Gotlib, 2005), a result uniquely predicted by the emotion context insensitivity view. Similarly, in a small sample, blunted autonomic reactivity to both positive and negative imagery scripts predicted a worse response to antidepressant treatment (Fraguas et al., 2007).

Finally, the emotion context insensitivity (ECI) view of MDD characterizes its core affective pathology in terms of a generalized blunting of NA and PA reactivity to negative and positive stimuli, respectively (Rottenberg, Gross, & Gotlib, 2005). This view is supported when the evidence for positive attenuation is combined with evidence of reduced NA reactivity in MDD (Allen, Trinder, & Brennan, 1999; Dickens, McGowan, & Dale, 2003; Lader & Wing, 1969; Peeters, Nicolson, Berkhof, Delespaull, & deVries, 2003; Rottenberg, Gross, et al., 2002; Rottenberg, Wilhelm, Gross, & Gotlib, 2002; Thomas et al., 2001). Like the others, the ECI view ascribes functional significance to generalized low PA and NA reactivity. However ECI predicts a more generalized pattern: those depressed persons with the lowest PA and NA reactivity across all stimuli (both positive and negative) will have the worst MDD course, uniquely predicting that low NA reactivity will predict a more pernicious MDD course. In favor of the ECI view, it was recently shown that relapse in remitted MDD patients was predicted by lower emotional reactivity to a mood induction (Kovacs, Rottenberg, & George, 2009).

Despite growing appreciation of the salience of emotional reactivity for psychological functioning and the availability of models that make predictions about the relation of emotional reactivity to MDD course, empirical investigations on this topic are scarce, equivocal, and methodologically heterogeneous (i.e., emotion assessed with omnibus self-report vs. multi-method experimental assessments; see Morris et al., 2009 for a review). Given limitations in previous work, our main goal was to conduct a comprehensive assessment of the relationship between emotional reactions to everyday life events and subsequent MDD course. The present study was an longitudinal extension of (Peeters et al., 2003) cross-sectional report that used an intensive and extensively validated field method (Experience Sampling Method; ESM; deVries, 1992; Ebner-Priemer, & Trull, 2009) over six days to generate an ecologically valid and reliable estimate of NA and PA reactivity for each participant. To address a clinically important outcome, we assessed whether emotional reactivity (computed as a within-subject independent variable) predicted remission from MDD over 18 months of follow-up. To avoid confounding of PA and NA reactivity by antidepressants (e.g., Dichter, Tomarken, Freid, Addington, & Shelton, 2005), participants were un-medicated during the ESM protocol. Finally, to limit potential for variations in treatment modality to confound the predictive power of emotional reactivity, participants were enrolled in a common treatment protocol (pharmacotherapy with supportive psychotherapy) administered in the same setting.

Given the dearth of prior prospective designs, we based predictions on the strength of the cross-sectional evidence supporting the ECI model (see Bylsma et al., 2008), specifically, that those depressed persons with the lowest PA and NA reactivity to all events (both positive and negative) will have the worst MDD course. Because the ECI model predictions subsume those of the other two models, all models are tested when testing the ECI model. We examined the predictive relation between emotional reactivity to everyday life events and MDD course, as indicated by prediction of (1) improvement in depression symptomatology and (2) full remission from MDD, a more stringent, and arguably more clinically important indicator (Judd, Paulus, Wells, & Rapaport, 1996).

Method

Participants

Forty-seven depressed participants were recruited from patients seeking treatment at the local community mental health center (CMHC) or the outpatient clinic of the regional psychiatric hospital in Maastricht, the Netherlands. Inclusion criteria at entry were age between 18 and 65 years, a primary diagnosis of major depressive disorder, as assessed with the Structured Clinical Interview for DSM-IV (SCID-1; First, Spitzer, Gibbon, & Williams, 1995) by the first author, and a score of ≥18 on the 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1967). Exclusion criteria at entry were substance abuse in the last six months, psychosomatic symptoms, bipolar disorder, and insufficient Dutch fluency. Current antidepressant use was also an exclusion criterion. In cases where previously prescribed antidepressants were judged clinically ineffective, these drugs were discontinued and participants were allowed to participate in the study after a medication-free interval of at least 1 week (this applied to 5 participants, none of whom used fluoxetine). Use of previously prescribed low-dose benzodiazepines was allowed (8 participants). The local medical ethics committee approved the study. Participants provided written informed consent and were paid $30 for participating in the initial ESM-study; there was no payment for follow-up measurements.

Ambulatory sampling procedure

The ESM was used to collect data from participants at selected moments during their daily activities (for more detail, see Peeters et al., 2003). Participants received auditory signals (beeps) from
a wristwatch programmed to emit 10 beeps daily between 7:30 a.m. and 10:30 p.m., at semi-random intervals of approximately 90 min. After each beep, participants completed paper-and-pencil based self-report forms concerning recent events and current affective state. Participants completed ESM reports for 6 consecutive days, including a weekend, resulting in a maximum of 60 samples from daily life for each participant. During a briefing session, study aims and procedures were explained. A research assistant called the participants during the first day to answer questions or clarify unclear issues about the procedure. ESM booklets were returned after the 6-day study period, where they were checked for legibility and missing data.

Compliance with the procedure was good. The compliance criterion for inclusion in the analyses (more than 20 ESM reports completed within 25 min after the programmed time of the beep) was met by all but one participant, who was excluded from analyses. Only 1 participant completed < 30 reports, whereas 95% of the participants provided between 40 and 60 valid ESM reports. Mean number of valid responses was 49. This compliance percentage (valid responses to 82% of the total beeps), though slightly lower than healthy controls (89%) in the same study, was similar to compliance levels observed in other studies using this sampling schedule (van Eck, Nicolson, & Berkhof, 1998).

**Measures of emotion**

Momentary emotional states were assessed at each beep with 20 adjectives rated on 7-point scales (1 not at all to 7 very). From the item pool previously used by our research group (Barge-Schaapveld, & Nicolson, 2002; Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001; van Eck et al., 1998), we included affect terms that varied in the pleasantness-unpleasantness as well as the arousal dimension. Principal components analyses with varimax rotation on mean scores aggregated per person and on within-person z scores identified two emotion factors with eigenvalues greater than 1. These factors accounted for 81% of the total between-person variance in mean emotion levels and 46% of the within-person variance in emotional states. Ratings on the items anxious, irritated, restless, tense, guilty, edgy, distracting, and agitated were averaged to form a negative affect (NA) scale. Ratings on the items energetic, enthusiastic, happy, cheerful, talkative, strong, satisfied, and self-assured were averaged to form a positive affect (PA) scale. The items gloomy, lonely, tired, and calm had similar loadings on each of the two factors and were therefore excluded from the NA and PA scales. Reliabilities of these scales were retrieved from a three-level random effects model where items were nested within beeps and beeps within persons (Bryk & Raudenbush, 1992). Reliabilities of the person level intercepts were high (NA = .99; PA = .98). Reliabilities at the beep level for use in discrimination among beeps within the same person were 0.74 for PA and 0.57 for NA.

**Measures of daily events**

After responding to the question “Did you experience a positive event or situation since the previous beep?”, participants who answered affirmatively were asked briefly to describe the event in their ESM booklet and to rate the event on several appraisalal dimensions, including stressfulness (1 not at all to 7 extremely). These questions were then repeated with respect to “a negative event or situation.” Although participants were instructed to report only external events or situations that actually took place in their daily environment in the preceding interval, some event reports clearly referred to internal states (e.g., current ruminations about past events, personal health concerns). Following pre-established criteria, the research team identified such internal events by consensus and omitted them from subsequent analyses, to avoid confounding of event and mood measures. In our sample, 9% of the positive event reports referred to internal states, whereas 25% of the negative events referred to internal states. Our sample reported a total of 755 external events. Of the 440 positive events reported, the most common category involved the depressed participant’s social network (44%), followed by household chores and shopping (13%), recreation and relaxation (12%), personal care (11%), and work (5%). 18% of positive events occurred outside these contexts. Social network events were also common (42%) among the 315 negative events, followed by personal care activities (29%), household and shopping (9%), work, recreation, and transportation (each less than 5% of the total), and other contexts (10%).

Briefly summarized, in a cross-sectional report of these data, Peeters et al. (2003) found that depressed and healthy reported similar frequencies of negative events, but depressed appraised such events as significantly more unpleasant, stressful, and important. Depressed reported a lower frequency of positive events and also rated these events as less pleasant and more stressful, but similarly important, compared to healthy participants.

**MDD treatment and assessment of MDD outcome**

Immediately after the ESM sampling week, all participants entered a naturalistic treatment phase. Patients received a combination of pharmacotherapy and supportive psychotherapy. MDD treatment was administered according to American Psychiatric Association guidelines (APA, 2000b). Typically, sessions were weekly and were decreased in frequency following agreement between therapist and participant. Therapies in the CMHC typically last between 15 and 20 therapy sessions. Participants were prescribed serotonergic antidepressants in flexible dosage depending on participants’ response and tolerance. In case of non-response, medication was switched to venlafaxine or a tricyclic agent, and lithium was added in case of enduring non-response. No participants received MAO-inhibitors or ECT. Patient compliance with treatment and interview procedures was excellent; only 2 participants, while still fully symptomatic, were lost over the follow-up by declining further contact; these participants did not differ significantly from the remaining sample of 44 participants on clinical and emotional reactivity variables.

Clinical outcome was measured monthly for 18 months with the HDRS as assessed in telephone interviews conducted by a trained research assistant. A random sample of 16 interviews was simultaneously rated by the first author throughout the study period to check the quality of HDRS assessments; the interrater reliability estimate for total HDRS scores was .96 (95%CI = .86—.99). Monthly HRDS scores were used to create both continuous and categorical outcome measures. Remission from MDD was defined as 2 consecutive monthly HDRS scores of ≤7 (Frank et al., 1991).

**Statistical analysis**

Individual emotional responses to positive and negative events were obtained from a three-level model (Bryk & Raudenbush, 1992) for mood (NA or PA) scores nested within days nested within subjects. Here, the mood at a certain moment (beep) was predicted by the person-specific mood mean level and the person-specific reactivity to a positive/negative event. Person-specific reactivities were estimated from a mixed effects model in which they were modeled as randomly varying. Person-specific estimates were obtained by empirical Bayes estimation (Morris, 1983) and performed with the MIWin package (Goldstein et al., 1998). Thus, we created for each participant 4 new variables consisting of their emotional (NA and PA) reactions to negative and positive daily
events. ANCOVAs were used with the person-specific reactivity to a positive/negative event as the predictor and the HDRS scores after 1, 2, 3, 6, 12, and 18 months of follow-up as the criteria. To provide a more stringent test, traditional clinical predictors of MDD course (duration of the current depression episode at entry, HDRS score at entry) as well as dispositional mood (the person’s mean mood level, NA or PA) were included in regression models as predictors.

To examine whether emotional reactivity predicted the probability of achieving full clinical remission over the follow-up, the Cox proportional hazards model was applied, with the same control variables included. All tests were two-sided. Statistical significance was assessed with the Wald test.

**Results**

**Demographic and clinical characteristics**

Depressed participants suffered from moderately severe index episodes with a fairly long duration (M = 20 months). In addition to their primary diagnosis of MDD, 21 participants (46%) had a secondary axis-I diagnosis, mainly anxiety disorders. Because we found no differences between participants with or without a co-morbid anxiety disorder, our results pertain to the sample as a whole. As expected, across the sample positive events elicited increases in PA and decreases in NA, whereas negative events elicited increases in NA and decreases in PA. Sample demographic, clinical characteristics, and mean emotional reactivity to daily events are displayed in Table 1. Correlations between the emotional reactivity measures, and demographic and clinical variables are shown in Table 2. Participants with longer current episodes or reporting more number of negative daily events showed lower NA reactivity following positive events. Other correlations were non-significant. There was no gender difference in the four emotional reactivity measures (r’s ranging from −1.3 to 1.3, df = 44, all p’s > .05).

**Prediction of symptomatic change**

Mean HDRS scores after 1, 2, 3, and 6 months were 15.3 (S.D. 6.8), 14.9 (S.D. 6.3), 13.5 (S.D. 7.4), and 11.9 (S.D. 6.5) respectively. To test whether emotional reactivity predicted changes in depression symptom levels during the 18 month follow-up period, we examined the association between HDRS scores and the reactivity for NA and PA following negative and positive events separately with multiple ANCOVAs. The results of these analyses are displayed in Table 3. The table shows the association between emotional reactivity and follow-up HDRS scores (after 1, 2, 3, 6, 12 and 18 months respectively) while controlling for baseline depression severity (HDRS), duration of current episode, and baseline mood. All four emotional responses to daily events predicted depression symptom severity after the first month of treatment, over and above the prediction offered by baseline depression severity, episode duration, and mean levels of reported mood. The observed pattern of results was consistent with the ECI model, in that intact emotional reactivity across valence and event types was associated with a more benign course of MDD. In contexts in which increases in emotion were observed — PA to positive events and NA to negative events — those depressed participants who exhibited the largest increases showed the largest decreases in depression symptoms at one month (the β’s in Table 3 are negative). Similarly, in contexts in which decreases in emotion were observed — NA to positive events and PA to negative events — those depressed participants who exhibited the smallest increases showed the smallest decreases in depression symptoms at one month (β’s in Table 3 are positive). Although a majority of the other follow-up analyses had β’s with nominal values that were also consistent with the ECI model, they

**Table 2**

Correlations between emotional responses and individual characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age</th>
<th>HDRS</th>
<th>Duration of current episode</th>
<th>No. of pos. events</th>
<th>No. of neg. events</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA response after neg-event</td>
<td>.20</td>
<td>.16</td>
<td>−.07</td>
<td>.15</td>
<td>.21</td>
</tr>
<tr>
<td>NA response after pos-event</td>
<td>.02</td>
<td>−.01</td>
<td>.19</td>
<td>.12</td>
<td>.19</td>
</tr>
<tr>
<td>PA response after neg-event</td>
<td>−.05</td>
<td>−.18</td>
<td>−.01</td>
<td>.07</td>
<td>−.06</td>
</tr>
<tr>
<td>PA response after pos-event</td>
<td>−.08</td>
<td>−.21</td>
<td>−.33</td>
<td>−.01</td>
<td>−.31</td>
</tr>
</tbody>
</table>

*p < .05.

**Table 3**

Association between depression symptom severity at follow-up and emotional responses.

<table>
<thead>
<tr>
<th>Follow-up at</th>
<th>1 month</th>
<th>2 months</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative events</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA reactivity</td>
<td>−3.04**</td>
<td>−1.13</td>
<td>−.94</td>
<td>−2.92</td>
<td>.70</td>
<td>−.56</td>
</tr>
<tr>
<td>Duration current episode</td>
<td>.09**</td>
<td>.02</td>
<td>.09</td>
<td>.07</td>
<td>.06</td>
<td>.06</td>
</tr>
<tr>
<td>Baseline HDRS</td>
<td>.48**</td>
<td>.47</td>
<td>.47</td>
<td>.01</td>
<td>−.25</td>
<td>−.29</td>
</tr>
<tr>
<td>Baseline NA</td>
<td>3.23**</td>
<td>1.73</td>
<td>−.68</td>
<td>.64</td>
<td>−.35</td>
<td>.89</td>
</tr>
<tr>
<td>PA reactivity</td>
<td>2.58**</td>
<td>.33</td>
<td>−.34</td>
<td>1.12</td>
<td>1.43</td>
<td>.09</td>
</tr>
<tr>
<td>Duration current episode</td>
<td>.10**</td>
<td>.03</td>
<td>.07</td>
<td>.03</td>
<td>.12</td>
<td>.06</td>
</tr>
<tr>
<td>Baseline HDRS</td>
<td>.68**</td>
<td>.65</td>
<td>.38</td>
<td>−.04</td>
<td>−.43</td>
<td>−.21</td>
</tr>
<tr>
<td>Baseline PA</td>
<td>−.94</td>
<td>−.68</td>
<td>−.56</td>
<td>−.49</td>
<td>1.03</td>
<td>−.06</td>
</tr>
</tbody>
</table>

| Positive events               |         |          |          |          |           |           |
| NA reactivity                 | 5.48**  | 1.84     | 1.89     | 5.41     | −.85      | 1.20      |
| Duration current episode      | .11**   | .02      | .09      | .07      | .10       | .06       |
| Baseline HDRS                 | .54**   | .52      | .49      | −.09     | −.26      | −.28      |
| Baseline NA                   | 6.72**  | 2.19     | 5.66     | .39      | −1.64     | 1.69      |
| PA reactivity                 | −2.56   | −3.02**  | −.72     | −.11     | 2.77      | .69       |
| Duration current episode      | .09**   | .03      | .07      | .03      | .12       | .06       |
| Baseline HDRS                 | .65**   | .53**    | .37      | −.05     | −.33      | −.19      |
| Baseline PA                   | .12     | −.85     | −.35     | −.80     | .63       | .05       |

*p < .01, **p < .05.

Note. Mean (SD) shown for continuous variables. HDRS = 17-item Hamilton Depression Rating Scale. NA = negative affect, PA = positive affect.
were not statistically significant at subsequent assessment points (with the exception of PA reactivity to positive events at 2 months).

**Prediction of remission from MDD**

Twenty-six of the MDD participants (57% of the sample) achieved full remission during the 18-month follow-up period. The median time to remission was 4 months (range 1–15 months). To examine whether PA- and NA reactivity to daily events predicted clinical remission of MDD over the follow-up period, a Cox proportional hazards model was used. The analysis, like that of the continuous analysis, was carried out while controlling for initial depression severity, episode duration, and baseline mean mood levels. The results are displayed in Table 4. Consistent with the ECI view, blunted NA reactions following negative events were significantly associated with a lower probability of remission over the follow-up period. The other emotional responses did not significantly predict MDD remission.

**Discussion**

Alterations in emotional reactivity are theorized to have etiological significance for MDD course. To our knowledge, this is the first study ever to find associations between ambulatory emotional reactions to naturally occurring negative and positive daily events and the subsequent clinical course of diagnosed MDD.

Our two major findings were both consistent with the ECI model. First, diminished reactivity to everyday life events predicted relatively higher depression severity levels during the first month of the follow-up period and this prediction held even when traditional clinical predictors of depression course and dispositional mood were statistically covaried. Because the relation between reduced reactivity and higher symptoms held across both valences and both types of events, the ECI model offered the most parsimonious overall account of the short-term symptom data.

Second, those individuals who exhibited reduced NA reactivity to negative life events were less likely to remit from MDD during the naturalistic treatment phase. This finding, too, is consistent with the ECI model, as the ECI model is unique in linking low NA reactivity to poor course. Given that residual depression symptoms are themselves known to be associated with significant functional impairment, including increased risk for depression relapse (Judd, Paulus, & Zeller, 1999), the prediction of full remission is a clinically salient finding.

Although our findings were consistent across both depression outcome measures, one important caveat is that emotional reactivity only predicted depressive symptoms at the earliest follow-up points and did not predict symptoms at subsequent follow-up points (with only one exception at the 2 month follow-up). Several hypothetical explanations for this finding can be given. Firstly, largest effects of both pharmacotherapy and psychotherapy for depression are typically seen within the first 4–6 weeks, which increases the chance to find significant associations during early follow-up only, especially in smaller samples like ours (Iardi & Craighead, 1994; Tang, Luborsky, & Andrusyna, 2002; Trivedi et al., 2006). More frequent (e.g., weekly) measurements of depression severity in this first stage of treatment may help to improve our understanding of the association between emotional responsivity and course. Secondly, these early and significant changes in clinical condition are generally the result of sudden gains in therapy (e.g., Tang & DeRubeis, 1999; Vittengl, Clark, & Jarrett, 2005); future research may address if, how, and why emotional reactivity is related to these sudden gains. It can be hypothesized that depressed individuals with larger emotional reactivity can profit more from interventions and interactions (e.g., non-specific factors like giving hope and understanding by their therapist) as introduced early in treatment. Moreover, it may be important to examine these phenomena in various treatment approaches given emerging evidence that different treatments are characterized by different mechanisms of change (Goldapple et al., 2004; Segal et al., 2006; Tang et al., 2009). Thirdly, as time progresses more (unmeasured) factors like newly occurring negative or positive events, or changes in social support may exert influence on long-term course thereby diluting the effects of emotional reactivity.

Although this study was novel in its use of ambulatory assessments of affect, many of the results are directly or indirectly commensurate with previous reports. Studies that measured affective reactivity retrospectively have also found blunted emotional reactivity to be associated with a worse outcome in MDD (Kasch et al., 2002; Moos & Cronkite, 1999; Spijker et al., 2001). Confidence in our findings is also increased by some convergence across different emotion response systems. For example, studies examining reactivity in peripheral and central nervous system responses have found that patients who exhibit more robust reactivity in anterior cingulate (Davidson, Irwin, Anderle, & Kalin, 2003), heart rate reactions (Rottenberg, Wilhelm, et al., 2002), and amygdala (Canli et al., 2005) following emotional stimuli have less severe MDD symptoms (but see also Siegle, Carter, & Thase, 2006).

Our results appear to conflict with (Cohen et al., 2008), who reported that increased next-day NA reactivity (but not same-day NA reactivity) predicted a worse early response to cognitive therapy. In an extension of this study, the authors reported that improvement of the participants’ clinical condition was associated with a decrease of NA reactivity to the number of negative daily events but also, commensurate with our findings, with an increase of NA reactivity to daily negative thoughts (Parrish et al., 2009). Upon a closer inspection, however, it is unclear whether divergent results are due to differences in the treatment regimen (cognitive therapy versus a combination of pharmacotherapy and supportive psychotherapy) or, perhaps more importantly, to major differences in experience sampling methodology. Indeed, one advantage of the present investigation over Cohen et al is that participants reported their emotional reactivity in close temporal proximity to recent life events, rather than reconstructing their reactivity at the end of the day. Indeed, end of day appraisals of a day’s worst event and mood may be problematic because this procedure invites contamination of mood reports by ruminative response styles or memory biases (Ebner-Priemer & Trull, 2009). This may also help to explain why next-day NA reactivity, which can be interpreted as a highly ruminative response, in the Cohen et al study predicted a worse response to treatment; high levels of rumination are associated with a less favorable MDD course (Nolen-Hoeksema, 2000).

This was the first study to find associations between intensively sampled ambulatory reactivity and MDD course; therefore, our results will require independent replication. One critical direction for future work will be to consider the underlying proximal

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**Table 4**

Association between achievement of remission and emotional reactions to daily events.

<table>
<thead>
<tr>
<th></th>
<th>b</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA reactivity</td>
<td>-.83</td>
<td>.51</td>
<td>2.67</td>
<td>1</td>
<td>.16–1.18</td>
<td>.10</td>
</tr>
<tr>
<td>PA reactivity</td>
<td>.35</td>
<td>.23</td>
<td>2.43</td>
<td>1</td>
<td>.91–2.21</td>
<td>.12</td>
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<td><strong>Negative events</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NA reactivity</td>
<td>.67</td>
<td>.25</td>
<td>6.91</td>
<td>1</td>
<td>1.18–3.21</td>
<td>.009</td>
</tr>
<tr>
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<td>1</td>
<td>.47–1.28</td>
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mechanisms accounting for why ambulatory reactivity predicts MDD course. At this early stage, we interpret these effects broadly within a functionalist view of emotion, in which robust emotional reactions to daily life events foster adaptation to environmental opportunities and threats. To the extent that emotional reactions serve an adaptive function, the better prognosis among depressed individuals who have larger increases in NA following negative events may reflect the relative integrity of their withdrawal motivational system. One might speculate that aversive increases in NA may prompt individuals to cope directly with undesirable events and situations, and by addressing these sources eventually decrease the high levels of NA that are characteristic of MDD (Clark, Watson, & Mineka, 1994). Greater emotional reactivity in the daily lives of individuals with MDD may also promote a better prognosis by stimulating a more active role in initiating productive and socially satisfying activities (Dimidjian et al., 2006). Further support comes from the study of Lethbridge and Allen (2008) who showed that a blunted decrease in PA after negative mood induction predicted relapse in remitted depressed participants.

The current study has several notable strengths. First, both MDD diagnosis and course were rigorously established using well-established interview-based instruments, whereas the principal outcome (remission) was determined on the basis of careful and frequent measurements. Second, none of the participants was using antidepressants during the ESM protocol, which rules out a pharmacological explanation of our findings. Third, participants provided multiple affect ratings over a range of daily contexts, which is likely to be a more reliable assessment of emotion reactivity than afforded by single point assessments. Finally, daily events almost certainly have more personal meaning to participants than do standardized experimental stimuli; this assessment of emotional reactivity was likely high in ecological validity.

This study also had some limitations. First, although all participants underwent antidepressant treatment according to state-of-the-art guidelines and supportive psychotherapy (APA, 2000b) and treatment was to some extent controlled, we did not assess many factors known to influence outcome, such as compliance with the antidepressant regimen (Keller, Hirschfeld, Demyttenaere, & Baldwin, 2002), quality of the therapeutic relationship (Zuroff & Aponte, 2002), and adherence to antidepressant regimen (American Psychiatric Association, 2000). Practice guideline for the treatment of patients with major depressive disorder (revision). American Journal of Psychiatry, 157(Suppl. 1), 1–45. Bange-Schaapveld, D. Q., & Nicolson, N. A. (2002). Effects of antidepressant treatment on the quality of daily life: an experience sampling study. Journal of Clinical Psychiatry, 63(6), 477–485.


