



## 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

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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-Gruoso, & 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, Delespaul, & 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  $\geq 18$  on the 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1967). Exclusion criteria at entry were substance abuse in the last six months, psychotic 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

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