Diurnal Mood Variation in Major Depressive Disorder

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Depression disturbs mood, but a clear picture of diurnal mood rhythms in depression has yet to emerge. This study examined variations in positive affect (PA) and negative affect (NA), two dimensions of mood that generate diurnal patterns among healthy individuals. Repeated measurements of NA and PA in daily life were obtained over 6 days from 47 depressed outpatients and 39 healthy individuals using the Experience Sampling Method. Relative to healthy individuals, depressed individuals exhibited increasing PA levels during the day with a later acrophase. In contrast, depressed persons’ NA exhibited a more pronounced diurnal rhythm and was more variable from moment to moment than healthy individuals'. Ambulatory mood measurements in depression suggest distinct diurnal disturbances of positive and negative affect.

Keywords: depression, affect, variability, rhythm, daily life

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) classifies depression as a Mood Disorder (American Psychiatric Association, 1994). Indeed, durable disturbance of mood is one of the most salient features of major depressive disorder (MDD). DSM-IV diagnostic criteria specify symptoms of at least 2 weeks' duration implicating both deficient positive affect (i.e., anhedonia) and excessive negative affect (i.e., sad mood, guilt). Consistent with these diagnostic criteria, depressed patients typically report low levels of positive affect and high levels of negative affect on questionnaire and interview measures (e.g., Clark, Watson, & Mineka, 1994). Despite the prominence of mood disturbance in MDD, we have remarkably little systematic information concerning how depression alters the dynamics of mood states as they unfold in everyday life.

Clinical observers have often noted that depressed persons exhibit changes in mood throughout the day (e.g., morning worse) and abnormalities in the moment-to-moment variability of mood. In particular, changes in mood throughout the day appears to be a common accompaniment of depression, often present for many days within an episode of MDD (Gordijn, Beersma, Bouhuys, Reinvink, & Van den Hoofdakker, 1994; Leibenluft, Noonan, & Wehr, 1992). In fact, a morning worse pattern is incorporated in formal criteria for the melancholic subtype of MDD, though patients with other forms of depression also appear to report such a pattern (Leibenluft et al., 1992). Moreover, a change of mood throughout the day has also been demonstrated to have clinical relevance, predicting response to biological treatments like sleep deprivation (Gordijn et al., 1994) and pharmacotherapy (Carpentier, Kupfer, & Frank, 1986).

Several recent investigations have made systematic comparisons between mood variability in depressed individuals with that of different control groups. These studies have varied in methodology and have generated conflicting findings. Cowdry et al. (1991) examined mood using visual analog scales (VAS) twice daily for two weeks in participants with MDD, borderline personality disorder, and healthy controls. The depressed participants were characterized by low absolute mood levels and low variability between and within days, indicative of low mood levels without much change during the study period. Low ultradian variability of mood, based on four daily VAS-measurements during three consecutive days, was found in depressed inpatients in comparison to healthy subjects who were examined in their daily lives (Wefelmeyer & Kuhls, 1996). Based on hourly VAS ratings during one 24-hour study period, a more recent study (Golier, Yehuda, Schmeidler, & Siever, 2001) also reported low mood variability in MDD in comparison to a group of participants suffering from PTSD and a healthy control group. However, in yet another study (Hall, Sing, & Romanoski, 1991), depressed inpa-
tients reported greater mood variability than healthy participants based on hourly VAS ratings during a 12-hour study period. Finally, depressed participants reported more mood variation based on daily mood reports over a study period of 14 months (Eastwood, Whitton, Kramer, & Peter, 1985).

Limitations of Previous Studies

Extant studies of mood variation in depression have not only yielded conflicting findings, they have also often lacked important methodological desiderata. The most critical problems have concerned: (a) measurement of mood; (b) unrepresentative assessment context; and (c) medication confound. We address each of these areas in turn.

One limitation of prior work stems from the measurement of mood with unidimensional VAS scales. Typically, mood is measured by instructing participants to place a mark along a 100-mm line at the point that best represents their mood state (either past or present). The extremes of the scale are labeled as “worst ever felt” and “best ever felt.” Recent investigations of the factor structure of mood experience have shown little support for unidimensional models and converged on two-factor models, often labeled positive affect (PA) and negative affect (NA) (e.g., Watson & Tellegen, 1985). Several related theoretical perspectives have highlighted the connections between PA and NA and broader affective systems governing approach and withdrawal motivation, respectively (e.g., Davidson, 1992; Depue & Collins, 1999; Gray, 1973; Watson, Wies, 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, tension, and guilt (Watson et al., 1999).

Moreover, because PA and NA are known to generate distinctive patterns of diurnal variation in healthy participants (e.g., Murray, Allen, & Trinder, 2002; Watson et al., 1999), separate measurement of PA and NA is critical for understanding diurnal mood variation in depression. Daily PA typically exhibits morning increases and evening decreases, mirroring circadian rhythms in body temperature and sleep-wake timing (Boivin et al., 1997; Clark, Watson, & Leeka, 1989; Murray et al., 2002; Watson et al., 1999). This characteristic \( \cap \)-shaped pattern of daily PA may reflect an evolutionary past in which the availability of rewards has been greatest during daylight hours. In sharp contrast, NA activity shows little evidence of a strong endogenous rhythm (Clark et al., 1989; Murray et al., 2002; Watson et al., 1999). Alternatively, the NA system is reactive, remaining low and constant throughout the day in the absence of threat or danger, and mobilizing whenever threats are detected.

A second limitation of prior work on diurnal mood variation in depression has been the measurement of mood in inpatient settings (e.g., Cowdry et al., 1991; Golier, Yehuda, Schmeidler, & Siever, 2001; Gordijn et al., 1994; Welfelmeyer & Kuhs, 1996). In the past, some authors have called for rigorous control of environmental influences (e.g., constant routine protocols) in mood studies (Hall et al., 1991; Haug & Wirz-Justice, 1993). Although such approaches may standardize location, activities, and interpersonal contacts, internal factors like rumination cannot be controlled; in fact, such internal factors may exert an even greater influence on mood when subjects are isolated from their daily contexts. Moreover, it must be kept in mind that inpatient settings are designed to remove patients from their regular daily environment and routines. These measurement contexts are thus likely to be highly unrepresentative of the emotional environments that depressed persons typically inhabit. Thus, mood variation data obtained in inpatient settings may not correspond to the mood variations depressed persons actually experience in everyday life (e.g., Welfelmeyer & Kuhs, 1996); this problem of ecological validity suggests the critical need for ambulatory monitoring of mood states in depressed patients.

A third limitation of several studies is that mood measurements have been concurrent with administration of antidepressant medications (e.g., Benedetti, Barbini, Campori, Colombo, & Smeraldi, 1998; Hall et al., 1991; Leibenluft et al., 1992; but see Cowdry et al., 1991; Golier et al., 2001). Antidepressants presumably exert their effects by increasing positive affect and decreasing negative affect. It has recently been shown that antidepressants have specific effects on levels of positive affect and negative affect (Dichter, Tomarken, Freid, Addington, & Shelton, 2005; Tomarken, Dichter, Freid, Addington, & Shelton, 2004), and it is also likely that antidepressants influence diurnal variations in mood, making them potentially a serious confound when studying mood variation in depression.

The Present Study

The current study, as a comprehensive assessment of mood variation in depression, featured these methodological desiderata. First, to address separate patterns of diurnal variation of PA and NA, we conducted separate measurements of these mood states in depressed and nondepressed individuals. Second, to measure ambulatory mood variation during the flow of everyday life we used the Experience Sampling Methodology (ESM; deVries, 1992). Finally, to avoid medication confounds, we sampled mood only in patients who were currently not taking antidepressant medications.

Using multilevel regression, we compared depressed and nondepressed participants’ patterns of diurnal variation in PA and NA. Based on the premise that PA is more tied to diurnal rhythms than NA, and on evidence that depression disturbs both positive affectivity and circadian rhythms (e.g., Boivin, 2000; van Londen et al., 2001), our primary hypotheses were that depressed individuals would (a) report lower PA, and (b) would exhibit a different diurnal pattern in PA. Concerning the latter, we specifically examined if the timing of the maximum value (acrophase) of PA was different in both groups. In chronobiological research, abnormalities in timing of the acrophase are considered as an important element of dysregulated circadian rhythms (Provencio, 2005). Given the weaker diurnal regulation of the NA system, we had no strong predictions regarding diurnal NA in depression (although we expected depressed individuals to report higher NA levels overall). Given older suggestions that diminished mood variability is associated with poorer clinical functioning (reviewed in Haug & Fahndrich, 1990), we examined the association between overall levels and within-day variability of PA and NA, and severity and duration of the current episode in the depressed group.
Method

Participant Recruitment and Selection

Forty-seven participants diagnosed with MDD were recruited among individuals seeking treatment at the community mental health center and the outpatient clinic of the local psychiatric hospital in Maastricht, the Netherlands. The main inclusion criterion was a primary diagnosis of MDD, as assessed with the Structured Clinical Interview for DSM-IV (SCID-I; First, Spitzer, Gibbon, & Williams, 1995) by a research psychiatrist (F.P.). Information on length of the current depressive episode and family history for mood disorders was also obtained during this interview. Entry was restricted to individuals between 18-65 years of age with a 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) score of ≥18, indicating at least moderate severity of MDD. Exclusion criteria were current substance abuse, psychotic symptoms (both assessed with the SCID), and insufficient fluency in Dutch. None of the participants was using antidepressants, but use of low-dose anxiolytic drugs (which applied to eight participants) was allowed during the study. To exclude any possible influence of benzodiazepine usage, the analyses were repeated after exclusion of the eight benzodiazepine-users. All significant findings remained unchanged. The depressed participants completed the Beck Depression Inventory (BDI; Beck, Ward, & Mendelson, 1961).

Thirty-nine healthy participants, matched as a group to the patient sample for gender and age, were recruited from available research pools, academic staff, and through an advertisement in a local newspaper. Additional exclusion criteria for the healthy participants were a lifetime history of any DSM-IV axis-I disorder (assessed with the initial screening section of the SCID), or any inpatient treatment for an Axis I psychiatric disorder in a first-degree relative. Both healthy and depressed participants completed the Symptom Checklist (SCL-90; Derogatis, Lipman, & Cori, 1973).

The study was approved by the local medical ethics committee, and after complete description of the study to the subjects, written informed consent was obtained.

Procedure

ESM was used to collect data from participants at selected moments during their daily activities. Participants received auditory signals (beeps) from a wristwatch programmed to emit 10 beeps between 7:30 a.m. and 10:30 p.m. each day, at semirandom intervals of approximately 90 minutes. After receiving a beep, participants completed self-report forms concerning current mood.1 Every day, participants noted at what time they had fallen asleep the previous evening and awakened in the morning. Furthermore, they rated subjective sleep quality on a 7-point scale (1 = very poor, 7 = very good). Participants completed ESM reports for 6 consecutive days, including a weekend. During a briefing session, study aims and procedures were explained. In a final session, the ESM booklets were checked for legibility and missing data.

Compliance with the procedure was generally good. Participants included in the analyses completed an average of 85% of all possible responses within the time limit, resulting in an average number of valid responses of 50.7 per subject. The criteria set for inclusion in the analyses (more than 20 ESM reports completed within 25 minutes after the programmed time of the beep) were met by all but one subject (from the depressed group), who was excluded from the analysis. Only one participant completed <30 reports, whereas 95% of the participants provided between 40-60 valid ESM reports. Mean number of valid responses was somewhat higher in the healthy than in the depressed group, 53.2 vs. 48.6; t(84) = 3.3, p = .003.

Mood Assessment

Momentary mood states were assessed with 16 adjectives rated on 7-point scales (1 = not at all, 7 = very). We chose to include items typical of pleasantness-unpleasantness as well as activation or arousal dimensions because these seemed necessary in order to capture clinically relevant aspects of daily emotional experience in major depression. We did not use the PANAS-scales (Watson & Clark, 1988) as they contain “pure” activation items (see for a discussion; Watson et al., 1999), but relied on items that were used previously by our research group in different populations (Barge-Schaapveld & Nicolson, 2002; Myin-Germeys et al., 2003; Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001; Peeters, Nicolson, & Berkhof, 2003; Peeters, Nicolson, Berkhof, Delespaul, & deVries, 2003; van Eck, Nicolson, & Berkhof, 1998). As expected, a factor analysis of mood states yielded a two-factor solution: principal components analysis with varimax rotation on mean scores aggregated per subject and on within-subject z-scores identified two mood factors with eigenvalues greater than 1. These factors accounted for 81.1% of the total variance in subject mean scores and 46.1% of the variance in within-subject z scores.

Ratings on the items anxious, irritated, restless, tense, guilty, irritable, easily distracted, and agitated were averaged to form a NA scale (Cronbach’s alpha = .91 based on all 4535 ESM reports; item loadings on factor 1 ranged between .66 and .88, loadings on factor 2 between −.16 and −.40). Ratings on the items energetic, enthusiastic, happy, cheerful, talkative, strong, satisfied, and self-assured were averaged to form a PA scale (Cronbach’s alpha = .95 based on all 4535 ESM reports; item loadings on factor 1 between −.08 and −.42, loadings on factor 2 between .73 and .92). As expected, correlations between PA and NA based on raw data were relatively low, r = −.19, p < .001 for depressed and r = −.33, p < .001 for healthy subjects.

Statistical Analysis

We applied multilevel analyses using the program MLwiN (Goldstein et al., 1998) to examine diurnal patterns of PA and NA. The multilevel model is a variant of multiple regression appropriate when the data have a nested structure. In this study, we had three levels of nesting: the beep level at which the ESM observations were taken, the day level, and the person level. For PA and NA, we subsequently fitted two models. In the first model, we examined the effects of DEP (depression, coded 1 for depressed participants and 0 for healthy controls), DS (duration of sleep in minutes), and SQ (sleep quality) on mood states. At the beep level, the i-th mood score at day j of subject k was modeled by a quadratic function of time: Moodijk = β0ijk + β1ijk Timeijk + β2ijk TimeSqijk + εijk,

with β0ijk representing the intercept of subject k at day j, β1ijk the linear time effect, and β2ijk the curvature of the fitted diurnal function. At the day level, the intercept β0i was related to variables DS and SQ:

β0i = γ0i + γ1i DSi + γ2i SQi + εi,

and at the person level, the intercept γ0i the linear effect β1i, the quadratic time effect β2i, and the day-level effects γ1i and γ2i were related to group status DEP:

γ0i = δ0i + δ1i DEPi + εi;

γ1i = δ1i + δ1i DEPi;

γ2i = δ2i + δ1i DEPi;

γ1i = δ1i + δ1i DEPi;

1 In these forms, participants were also asked briefly to describe any positive and/or negative event that may have taken place since the last ESM report (see for a detailed description; Peeters, Nicolson, Berkhof et al., 2003). As controlling for covarying event occurrence did not influence the results, they were removed from the final statistical model.
$$\gamma_{ik} = \delta_{i0} + \delta_{i1}, \text{ DEP}_i.$$  

We tested whether the regression coefficients $\delta_{i0}, \ldots, \delta_{i0}, \delta_{i1}, \ldots, \delta_{i1}$ were different from zero and also tested whether the regression coefficients were different for depressed versus healthy subjects, i.e., whether the differences $\delta_{i1} - \delta_{i0}, \ldots, \delta_{i1} - \delta_{i0}$ were different from zero.

The linear effect $\beta_{i0}$ can be interpreted as the change in mood throughout the day, but this interpretation is somewhat complicated because the slope is nonconstant. A different interpretation stems from the relation between the effect $\beta_{i0}$ and the time of day at which mood reaches its maximum value (acrophase) being $-1 \times \beta_{i0} / 2 \beta_{i1}$. We can see that if depressed and healthy controls have the same curvature (i.e. $\delta_{i1} = 0$), linear effects $\beta_{i1}$ in the two groups directly correspond to acrophase time positions. Therefore, in the restricted model with $\delta_{i1}$ set equal to 0, we can check for an acrophase shift by testing null hypothesis $H_0$: $\delta_{i1} = 0$.

The residual $e_{ijk}$ is a person-level deviation from the average mood score, the residual $e_{ij}$ is a day-level deviation from the person’s average mood score, and $e_{ikt}$ is a beep-level residual. The contribution of each of these three residuals to the total variation in the data is expressed by the relative magnitude of the variances $\var(e_{ijk}), \var(e_{ij}), \var(e_{ikt})$. A relatively large person-level variance, for instance, indicates that average mood varies strongly from one person to another. We examined whether the beep, day, and person level variance were different for depressed and healthy controls. Besides, we examined whether the beep level variance was associated with DS and SQ. We allowed consecutive beep-level residuals to be autocorrelated and assumed that the correlation decreases exponentially with the length of the interval between consecutive sampling points.

In a second model for depressed participants only, we assessed the effects of BDI (severity of depression), DCE (duration current episode), and SCL (SCL-90 anxiety subscale) on mood and the beep level variance.

The variables Time, DS, SQ, BDI, DCE, and SCL were centered around the grand mean, and TimeSq was centered around the grand mean and around time. The hypotheses about the fixed effects were tested by dividing the fixed effect by its standard error yielding a normally distributed variable. Two-tailed tests were used even when hypotheses were directional. Given the multiple comparisons, the significance level was set at alpha = .01. The hypotheses about the beep level, day level, and person level variance were tested using the likelihood ratio (LR) test (Bryk & Raudenbush, 1992).

**Results**

The final sample consisted of 46 depressed and 39 healthy participants.² Demographic and clinical characteristics for the two groups are presented in Table 1.

Scores on the BDI and HDRS indicate moderate depression severity in the depressed group. In addition to the primary diagnosis of MDD, 21 patients (46%) had a secondary Axis I diagnosis, as follows: generalized social phobia ($N = 9$), dysthymic disorder ($N = 5$), panic disorder with agoraphobia ($N = 4$), posttraumatic stress disorder ($N = 4$), specific phobia ($N = 4$), bulimia nervosa ($N = 1$). Of these, four MDD participants had three or more Axis I diagnoses.

In the depressed participants, mean levels of PA and NA were 2.1 ($SD = .9$) and 2.8 ($SD = 1.3$), respectively. Mean PA and NA levels in the healthy participants were 4.5 ($SD = 1.1$) and 1.3 ($SD = 5$). In order to visualize the differences in daily patterns of PA and NA, we standardized the mood scores for each subject to minimize between-subject variance. Figures 1A and 1B show the resulting average standardized within-subject scores for PA and NA over the course of the day in the depressed and healthy groups. We present the results of the multilevel analyses for PA and NA in Tables 2 and 4, respectively. Values in the model are computed for depressed and healthy participants. The last column indicates group comparisons.

**Positive Affect**

Consistent with expectations, the average reported PA level was lower in depressed than in healthy participants (see Intersect Table 2). The pattern of diurnal variation of PA in depressed and non-depressed participants is displayed in Figure 1A. Depressed individuals exhibited a linear increase in PA over the course of the day that was absent in healthy individuals (see Figure 1A and “Time” in Table 2).

Additionally, both groups exhibited a similar characteristic ∩-shaped diurnal pattern of PA (see Figure 1A and “Time²” in Table 2). We also examined if the timing of the acrophase of PA was different in both groups. The acrophase in the depressed participants appeared to occur significantly later than in the healthy participants ($\beta = .022, SE = .006, z = 3.6, p < .001$). Based on our model, we computed that, on average, the acrophase in depressed participants occurred at 5:22 p.m., whereas the maximum levels of PA occurred at 3:35 p.m. in the healthy participants. In a second model, we investigated the association between clinical characteristics and PA in the depressed group. Those depressed participants with more severe current episodes reported the lowest levels of PA ($\beta = -.034, SE = .009, z = 3.7, p < .001$), there appeared a weaker association between longer current episodes and lower PA ($\beta = -.009, SE = .004, z = 2.2, p = .01$). The presence of anxiety symptoms (SCL-90 anxiety scale) was not related to PA ($\beta = .01, SE = .01, z = 1, p > .05$).

To place the diurnal PA data in a larger context, we estimated person-level, day-level, and beep-level variances of PA in the multilevel model before addition of independent variables. These data are presented in Table 3.

Variances at the person-level, the day-level, and at the beep-level were similar in the two groups.

Finally, consistent with suggestions that diminished mood variability is associated with poorer clinical functioning, longer current depressive episodes were associated with reduced beep-level PA variance in the depressed group ($\beta = .002, SE = .0004, z = 5, p < .001$). No association between depression severity and beep-level PA variance was observed.

**Negative Affect**

As expected, depressed participants reported experiencing higher levels of NA than healthy participants (see Intersect Table 4).

The pattern of diurnal variation of NA in depressed and non-depressed participants is displayed in Figure 1B. In contrast to the result for PA, depressed participants exhibited more pronounced diurnal variation in NA than healthy participants. As is apparent from Figure 1B, depressed persons’ daily NA was ∪-shaped function with a significant negative quadratic component (effect of

² There were no effects for gender and gender × group interactions on any of the mood variables.
“Time$^{2}$” in Table 4), with maximum NA during the late morning. This ∩-shaped pattern was absent in healthy participants’ diurnal NA (nonsignificant “Time$^{2}$” effect in Table 4). In addition, only the depressed group exhibited a negative linear pattern, with a significant decrease in NA levels over the course of the day (“Time” in Table 4).

In a second model, we examined the relation between clinical characteristics and NA in the depressed group. We found no association between severity and duration of the current episode and NA levels. However, higher scores on the SCL-90 anxiety subscale were associated with higher NA ($\beta = .045$, $SE = .017$, $z = 2.6$, $p < .01$).

Again, to place our diurnal NA data in a larger context, we estimated person-level, day-level, and beep-level variances of the multilevel NA model before addition of independent variables. These data are presented in Table 5.

At both the person-level and the beep-level, NA was more variable in the depressed group than in the group of healthy participants. The significant difference between the two groups in person-level variance indicates greater heterogeneity in average NA levels among participants in the depressed group. The larger beep-level variance in depressed participants indicates larger moment-to-moment variability in NA in the depressed group. The difference between the depressed and healthy group in day-level variability was not significant.

Finally, we examined the association between clinical functioning in the depressed group and NA variability at the beep-level. Although duration of the current episode was unrelated to beep-level NA variability, more severe depression ($\beta = .009$, $SE = .002$, $z = 4.5$, $p < .001$), more anxiety symptoms ($\beta = .01$, $SE = .002$, $z = 5$, $p < .001$), and lower sleep quality ($\beta = .026$, $SE = .008$, $z = 4.5$, $p < .001$) were associated with increased beep-level variability of NA.

### Discussion

The present study was the first to assess diurnal mood variations in depressed persons’ PA and NA using real-time reports obtained in everyday life settings. Depressed persons evidenced distinctive abnormalities in PA and NA relative to healthy subjects. Depressed persons’ PA increased over the course of the day with a backwards shifted acrophase, whereas NA exhibited increased diurnal variation and decreased over the course of the day. Moreover, PA in MDD was characterized by lower overall levels and reduced interindividual variation. In contrast, NA in MDD was characterized by higher overall levels, as well as both greater interindividual and moment-to-moment variance. The distinctiveness of these patterns of PA and NA variation merits special comment.

Consistent with previous reports (Murray et al., 2002; Watson et al., 1999; Wood & Magnello, 1992), we found that healthy participants’ diurnal PA exhibited a characteristic ∩-shaped diurnal pattern. Depressed individuals exhibited a similar pattern in PA, but their maximum levels occurred on average 107 minutes later. These findings provide the first evidence from fine-grained analyses of ambulatory PA for altered PA patterns in MDD, extending prior reports of diurnal rhythm disturbances in this disorder (Boivin, 2000; Peeters, Nicolson, & Berkhof, 2004; van Londen et al., 2001) and adding to the general literature on depression-related deficits in positive affectivity (Davidson, Pizzagalli, Nitschke, & Putnam, 2002; Depue & Collins, 1999).

Because the NA system has not been shown to generate a pronounced diurnal pattern in healthy subjects, we made no predictions concerning depression-related abnormalities in the diurnal variation of NA. Our unanticipated finding of increased diurnal variation of NA in depression is interesting and potentially important, but should be interpreted with caution until replicated. Most of our other NA findings may be viewed as reflecting overactivity
Figure 1. Diurnal patterns of mean PA (1A) and NA (1B) in depressed and healthy subjects (Note: The time points in the figures pertain to the middle of the 90-minutes intervals).
Table 2
Multilevel Estimates of Influences on Positive Affect (PA)

<table>
<thead>
<tr>
<th></th>
<th>MDD</th>
<th>Healthy</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>2.149 (.106)</td>
<td>4.526 (.149)</td>
<td>2.378 (.183)***</td>
</tr>
<tr>
<td>Time</td>
<td>0.029 (.004)***</td>
<td>0.007 (.004)</td>
<td>0.022 (.006)***</td>
</tr>
<tr>
<td>Time²</td>
<td>-0.007 (.001)***</td>
<td>-0.008 (.001)***</td>
<td>0.002 (.002)</td>
</tr>
<tr>
<td>Sleep quality</td>
<td>0.027 (.017)</td>
<td>0.024 (.027)</td>
<td>0.003 (.031)</td>
</tr>
</tbody>
</table>

Note. The analysis is based upon 4306 observations nested within 510 days, within 85 subjects. MDD = Major Depressive Disorder. *** p < .001.

in a withdrawal-related behavioral inhibition system in depression (BIS; Gray, 1973; Kasch, Rottenberg, Arnow, & Gotlib, 2002). That is, overactivity of the BIS would tend to generate high tonic levels of negative affect, and the ready detection of threats from environmental or internal cues, leading to easy perturbation and high moment-to-moment fluctuation in general distress and anxiety. Consistent with this BIS profile, depressed persons reported high overall levels of NA as well as high moment-to-moment variability in NA.

In addition, it was notable that the overall course of daily mood in depressed persons in thisambulatory context appeared to be more favorable as the day progressed. Depressed participants reported increased PA as well as decreased NA over the course of the day. This pattern is consistent with prior observations of “morning worst” mood in depression (Gordijn et al., 1994). Future research will have to address the associations between these daily patterns of PA and NA and response to biological treatments like sleep deprivation and pharmacotherapy.

We found clinically meaningful associations between mood states and disorder-related variables. As might be expected, PA and NA were respectively lower and higher in more severely depressed individuals. Perhaps more surprisingly, moment-to-moment variability of mood states was more abnormal in the clinically most severe cases. These data indicate the clinical significance of ambulatory mood measures and their potential for tracking severity and perhaps clinical course. Future studies should examine whether these alterations in mood variability are associated with the more unfavorable course that is frequently seen in more severely or longer depressed individuals (Spijker et al., 2002).

Although this study elucidated important differences in depressed persons’ diurnal patterns of NA and PA in the natural environment, the underlying sources of these differences will require additional clarification. The low levels of PA and high, fluctuating levels of NA in MDD fit well with neurobiological evidence for low BAS and high BIS activation in MDD (Davidson, 1992). Moreover, the shift in acrophase of PA levels is clearly consistent with other evidence of disturbed endogenous rhythms in this disorder, such as body temperature (van Londen et al., 2001), sleep rhythms (Boivin, 2000), and cortisol secretion (Deuschle et al., 1997; Peeters et al., 2004; Young et al., 1994). Despite this circumstantial evidence, however, we cannot yet assert that the mechanisms for these effects are in fact biological ones. For example, although we statistically controlled for a number of variables like occurrence of daily events and sleep patterns, it is possible that unmeasured environmental factors contributed to this difference in the diurnal pattern of PA. Clearly, the relative contributions of endogenous and exogenous factors to PA and NA dysregulation should be examined in future studies.

Four limitations of this study should be noted. Firstly, our study relied upon self-reported mood scales, which are vulnerable to floor and ceiling effects. Partially mitigating this concern, we conducted a number of residual analyses which suggested the absence of a floor effect of PA in both groups and a floor effect of NA in the depressed group. A floor effect cannot totally be ruled out for NA in the healthy participants as they regularly reported no experience of momentary negative affective states; the distribution of the NA beep level residuals was more peaked around the mode suggesting a possible floor effect. However, because the healthy group also showed robust and considerable NA residual variability, we think that a floor effect on the results is limited. Second, our self-report measures of mood, while good indices of PA and NA and readily measured in an ambulatory setting, are only one indicator of mood. To obtain a fuller picture of PA and NA, future studies will need to avail themselves of ambulatory techniques for measuring mood-relevant behavior and physiology (Wilhelm &

Table 3
PA Variance Components in the Multilevel Model

<table>
<thead>
<tr>
<th></th>
<th>MDD</th>
<th>Healthy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person level</td>
<td>.472</td>
<td>.825</td>
<td>.08</td>
</tr>
<tr>
<td>Day level</td>
<td>.024</td>
<td>.054</td>
<td>.13</td>
</tr>
<tr>
<td>Beep level</td>
<td>-0.119</td>
<td>-0.402</td>
<td>.34</td>
</tr>
</tbody>
</table>

Note. All variance estimates are statistically significant, p < .01, likelihood ratio test (Bryk & Raudenbush, 1992). The p-values pertain to differences between depressed and healthy participants. PA = Positive Affect; MDD = Major Depressive Disorder.

Table 4
Multilevel Estimates of Influences on Negative Affect (NA)

<table>
<thead>
<tr>
<th></th>
<th>MDD</th>
<th>Healthy</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>2.798 (.144)</td>
<td>1.349 (.51)</td>
<td>1.449 (.153)***</td>
</tr>
<tr>
<td>Time</td>
<td>-0.019 (.005)***</td>
<td>-0.004 (.003)</td>
<td>-0.015 (.005)***</td>
</tr>
<tr>
<td>Time²</td>
<td>-0.006 (.001)***</td>
<td>-0.001 (.001)</td>
<td>-0.005 (.001)***</td>
</tr>
<tr>
<td>Sleep quality</td>
<td>-0.026 (.019)</td>
<td>-0.014 (.015)</td>
<td>-0.012 (.025)</td>
</tr>
</tbody>
</table>

Note. The analysis is based upon 4306 observations nested within 510 days, within 85 subjects. MDD = Major Depressive Disorder. *** p < .001. ** p < .01.

Table 5
NA Variance Components in the Multilevel Model

<table>
<thead>
<tr>
<th></th>
<th>MDD</th>
<th>Healthy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person level</td>
<td>.896</td>
<td>.886</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Day level</td>
<td>.023</td>
<td>.023</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Beep level</td>
<td>.563</td>
<td>.184</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Note. All variance estimates are statistically significant, p < .01, likelihood ratio test (Bryk & Raudenbush, 1992). The p-values pertain to differences between depressed and healthy participants. NA = Negative Affect; MDD = Major Depressive Disorder.
ogy), sleep-quality, and moment-to-moment variability in mood (e.g. severity of depression and comorbid anxiety symptomatology). Furthermore, we found associations between clinical characteristics and different combinations of PA and NA levels, thereby obscuring mean-levels felt and best ever felt is the outcome of momentary and different diagnostic groups, which may otherwise be obscured by the dynamics of NA and PA to discriminate patterns between healthy individuals (Wood & Magnello, 1992). Inclusion of a variety of daily life settings can provide a useful and ecologically valid addition to other methods in mood research. Finally, a possible drawback of the naturalistic design employed in this study is the lack of control over participants’ compliance with the protocol because of the use of paper-and-pencil instead of electronic (e.g., palmtop-computer) data collection. Recently however, it was shown that with the use of a signal-contingent procedure with stratified random sampling times like in our study, verified compliance was 81% (Jacobs et al., 2005). As in the study by Jacobs et al. (2005), our participants were instructed to collect saliva samples (for later cortisol determination) and complete ESM booklets at the same time (Peeters, Nicolson, & Berkhof, 2003); it seems therefore reasonable to assume that accurately timed saliva samples were accompanied by accurately timed ESM reports. As Jacobs et al. (2005) argue, “cheating (for example, by taking and labeling the sample at the actual time, entering that time in the booklet, and then waiting to complete the booklet later) would cost considerably more effort than just fulling in the booklet at the right time” (p. 2440). Additionally, the strong associations between daily events and mood changes that are consistently reported in “paper-and-pencil based” ESM studies (e.g., Barge-Schaapveld & Nicolson, 2002; Myin-Germeys et al., 2001; Peeters, Nicolson, Berkhof et al., 2003; van Eck et al., 1998), advocate adequate compliance with these type of protocols.

The results of the current study have implications for existing conceptualizations and future research on mood in MDD. One question concerns the specificity of the observed patterns to depression. Diurnal variation has generally been considered to be a characteristic of MDD, but it can also be found in patients with other psychiatric disorders (Fahndrich & Haug, 1989) as well as in healthy individuals (Wood & Magnello, 1992). Inclusion of a psychiatric control group in future work to address the specificity of these effects to depression is clearly warranted. We believe our current results underscore the need for separate measurement of the dynamics of NA and PA to discriminate patterns between different diagnostic groups, which may otherwise be obscured by a unidimensional mood concept. Indeed, we believe it is likely that the application of a unidimensional mood concept is one of the factors that contributed to the conflicting results in prior studies of mood variability in MDD (Cowdry et al., 1991; Golier et al., 2001; Hall et al., 1991; Welfelmeyer & Kuhs, 1996). It is conceivable that the same unidimensional mood evaluation between “worst ever felt” and “best ever felt” is the outcome of momentary and different combinations of PA and NA levels, thereby obscuring meaningful underlying dynamics of PA and NA (Watson, 2000). Furthermore, we found associations between clinical characteristics (e.g. severity of depression and comorbid anxiety symptomatology), sleep-quality, and moment-to-moment variability in mood states in the depressed participants. However, previous studies did not report any within-group analysis which leaves open the possibility that differences in sample characteristics also may have contributed to previous conflicting results.

It has been postulated that the presence of mood lability in a depressed patient may be a good predictor of clinical response to various types of treatment (Gordijn et al., 1994; Haug & Wirz-Justice, 1993). Future studies should test if and how mean levels and variability of PA and NA in depressed patients are related to acute phase treatment response and long-term clinical course.

References


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