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A longitudinal study of diurnal mood variation in depression; characteristics and significance


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Abstract

The course of 39 depressed in-patients' daily mood was recorded by means of frequent self-ratings during their entire stay (in total 3718 days). The frequency of diurnal variations largely varies between subjects without clear dichotomy in 'diurnal' and 'non-diurnal' subjects and the occurrence of diurnal variations is rather irregular. Mood variability measures rather than average daily mood improvement correlate with the response to sleep deprivation. These observations do not support theories of chronobiological rhythm disturbances in depression. It is argued that depressed subjects largely vary in susceptibility to stimuli. Signals generated by the biological clock or by processes related to the sleep-wake cycle are considered examples of such stimuli.

Key words: Depression; Diurnal variation; Sleep deprivation; Mood variability; Self-rating; Longitudinal study

1. Introduction

Diurnal variation of mood, defined as an improvement or worsening of mood during a day, is often observed during depression. In the diagnostic criteria for melancholia in DSM-III-R, mood improvement over the day is one of the relevant symptoms; together with other symptoms such as anhedonia, weight loss and early morning awakening (American Psychiatric Association (APA), 1987). In addition, two interesting relationships support the relevance of the clinical use of diurnal mood variations. Positive correlations have been reported between the occurrence of diurnal mood variations during treatment and the antidepressant response to medication (Fähndrich, 1983; Haug and Stieglitz, 1990) and between diurnal variation on the day before total sleep deprivation (TSD) and the subsequent response to this intervention (Rudolf and Tölle, 1978; Roy-Byrne et al., 1984; Elsenga and Van den Hoofdakker, 1987; Reinink et al., 1990; Haug, 1992; Riemann et al., 1991).

Despite these facts, very few studies have been devoted to the recording of diurnal variations of mood over a distinct period of time. Except for a few longitudinal studies (Stallone et al., 1973;
Tölle and Goetze, 1987; Haug and Fähndrich, 1990) based on frequent self-ratings of mood, most studies on diurnal variations are just based on retrospective assessments. The present longitudinal study was performed to provide a detailed description of the phenomenon. The individual mood of thirty-nine depressed patients admitted to the closed ward of a psychiatric clinic was recorded for a total of more than 3700 days by means of self-ratings, obtained three times per day during their entire stay at the ward. Various mood variability measures including ‘diurnal variation’ were calculated. The criterion value used by Elsenga et al. (1987), to detect a clinical response to total sleep deprivation, was chosen for the definition of diurnal mood variation. The relevance of the value will be demonstrated.

By defining diurnal mood variation on the basis of the difference between mood scores in the morning and in the evening, it is implicitly assumed that mood changes monotonously in the course of the day. This assumption is tested by comparing actual self ratings in the afternoon to values obtained by linear interpolation of ratings in the morning and evening.

Mood variability measures are discussed in relation to severity of depression, retrospectively assessed diurnal variations and response to total sleep deprivation. The relationship between diurnal variation of mood and severity of depression is the subject of different opinions. Some authors reported that diurnal mood variations disappear with increasing severity of depression and that reappearance of diurnal mood variations is a sign of improvement (Middelhoff, 1967; Waldmann, 1972). Others did not find any correlation between diurnal mood variations and severity of depression (Haug and Fähndrich, 1990). Additionally, the results of retrospective ratings of diurnal mood variations are not always consistent with the results of prospective repeated measurements (Williams et al., 1975; Stieglitz et al., 1988; Leibenluft et al., 1992). The cause of this discrepancy remains unclear. The present study offers a large dataset to compare retrospective assessment of diurnal variations and longitudinally assessed mood variability measures. Recently, Reinink et al. (1993) discussed the relationship between diurnal mood variation, measured longitudinally, and the response to total sleep deprivation (TSD). They reported that the propensity of a patient to produce diurnal variations was correlated with the TSD response, while within patients the mood variation on the day prior to TSD did not seem to be important. The mood variability measures obtained in the present study are compared to TSD responses.

The 24-hour periodicity of diurnal mood variation (with morning lows most frequently reported) and its relationship with TSD supported ideas of a direct relationship between diurnal variation and sleep and/or with other 24-hour rhythms (Engel, 1957; Hall et al., 1964; Fähndrich, 1988; Beersma et al., 1991). Moreover, theories concerning the role of sleep (Wu and Bunney, 1990; Beersma and Van den Hoofdakker, 1992; Wehr, 1990) or chronobiological disturbances (Borbély and Wirz-Justice, 1982; Wehr and Wirz-Justice, 1981) in affective disorders often consider diurnal mood variations an important variable. Implications of the results of our longitudinal mood recordings, in combination with sleep deprivation results, will be discussed in terms of these processes.

2. Methods

Thirty-nine depressed patients of a closed ward were included in this study. The group constitutes a consecutive series except for dropouts. The closed ward is part of an academic hospital. The patient population is considered to be largely therapy-resistant at admission. The studied group participated in various studies on circadian rhythms and sleep deprivation (Reinink et al., 1993). Informed consent was obtained. The patients completed self-assessments of mood, by means of the Dutch version of Von Zerssen’s Adjective Mood Scale (AMS) (Von Zerssen, 1976; Von Zerssen, 1986; Elsenga, 1988), three times daily at 9 a.m., 5 p.m. and 10 p.m. The ratings range from 56, most severely depressed, to 0, not depressed. This scale is particularly suited for frequent use at short intervals (Von Zerssen and Cording, 1978). Patients started rating shortly af-
ter admission and continued to do so during almost their entire stay in the closed ward of our clinic. In our study of mood variability, only the depressed period of the patients was analyzed. This period ended, by definition, when no more days with AMS-ratings higher than 15 during the rest of the stay were observed.

Patients received various therapies including psychotherapies, sleep-wake interventions such as total or partial sleep deprivation, tricyclic antidepressives, benzodiazepines, neuroleptics, lithium and, in a few cases, electroconvulsive therapy. Because of the great diversity and combinations of therapies, and the present unknown effects of most of the therapies on diurnal mood variations, mood variability measures are calculated irrespective of treatment modalities with the exception of sleep deprivation. The first day after partial or total sleep deprivation was disregarded in all patients (n = 308 days) because of the known acute effects of sleep deprivation on mood (Rudolf and Tölle, 1978; Tölle and Goetze, 1987). Second-day responses to sleep deprivation have been reported in only very few studies (Wirz-Justice et al., 1976). These days were included.

The various measures of daily mood variability that were calculated are summarized in Table 1. Note the difference between MF (without criterion) and DV with a criterion of a difference of 6 or more points on the AMS between morning and evening score. The rating at 5 p.m. was not taken into account in establishing MF and DV.

Thirty-four patients took part in a Hamilton interview which took place at 9 a.m., within 2 weeks of admission (after a short acclimatization period), in order to rate the baseline severity of depression (Hamilton, 1967). For the present analysis, the 17-item Hamilton score has been calculated (the 17-item version does not contain the item concerning diurnal variation). A retrospective measure of diurnal variations was assessed on the basis of item 18 in the 21-item Hamilton Scale. A patient was considered 'non-diurnal type' when the average score for two raters on this item was less than 1 and 'diurnal type' when this score was 1 or more (Reinink et al., 1990). The type of 'diurnality' (e.g., better in the morning or in the evening) was recorded.

The relationship between mood variability measures and total sleep deprivation (TSD) response, the average response of each individual to the first two TSDs after days without DV were chosen. The individuals were subjected to TSD once a week. The response to TSD was defined as the difference score between the averaged depression scores of the day after and of the day before TSD corrected for the 'spontaneous' day-to-day variation. For details see Reinink et al. (1993). TSD responses after days without DV are available in 34 patients.

Various non-parametric statistical tests and ANOVA's were used to study interdependence of variables and possible differences between sub-

| Table 1 |
| Description of mood variability measures used in this study |
| Mood variability | Description |
| Mood fluctuation (MF) | difference between self-ratings of mood at 9 a.m. and 10 p.m.; a positive value means better mood in the evening than in the morning, a negative value refers to the opposite pattern |
| Mood fluctuation (AMF) | average difference between self-ratings of mood at 9 a.m. and 10 p.m. per individual over the complete depressive episode (or otherwise specified period) |
| Standard deviation (SD) of MFs | variability (standard deviation) of the differences in self-ratings of mood at 9 a.m. and 10 p.m. per individual |
| Diurnal mood variation (DV) | by definition, an absolute difference of at least 6 points between self-ratings of mood at 9 a.m. and 10 p.m. |
| Positive diurnal mood variation (pos DV) | a difference score of +6 or more between self-ratings at 9 a.m. and 10 p.m., representing better mood in the evening than in the morning |
| Negative diurnal mood variation (neg DV) | a difference score of −6 or less between self-ratings at 9 a.m. and 10 p.m., representing worse mood in the evening than in the morning. |

To examine the relationship between mood variability measures and total sleep deprivation (TSD) response, the average response of each individual to the first two TSDs after days without DV were chosen. The individuals were subjected to TSD once a week. The response to TSD was defined as the difference score between the averaged depression scores of the day after and of the day before TSD corrected for the 'spontaneous' day-to-day variation. For details see Reinink et al. (1993). TSD responses after days without DV are available in 34 patients.
groups. A probability level of $P < 0.05$ was the criterion for statistical significance for all tests.

3. Results

3.1. Patient characteristics

Diagnosis according to DSM-III-R and age and gender of the 39 patients included in the study are presented in Table 2. The average age of the group was 47.1 ± 12.3 (SD) years, ranging from 25 to 70 years. Stays ranged from 23 to 582 days. Patients had to complete questionnaires during their entire stay in order to be included in the analysis. Three patients were included although there were missing data, but these missing data covered only a minor part of their stay: two of them ended their participation 2 and 3 weeks before discharge respectively and the third started rating 4 weeks after admission. Eighteen patients reached the criterion for remission. The number of depressed days of each individual patient used for the analyses, after excluding the first day after TSD or PSD and days with missing morning or evening rating (total 882 days) is shown in column 5 of Table 2. The remaining total number of days included in the study is 3718. The mean Hamilton score at admission was 22.5 ± 6.2 (n = 34, patient Nos. 4, 10, 33, 34 and 38 in Table 2 are missing). The other patients showed patterns in between these extremes. Figure 2(top) shows the frequency distribution of the average daily mood fluctuations of the patients. In order to give an impression of the variability of mood fluctuations, the frequency distribution of the standard deviation of the MFs is shown in Fig. 2(bottom). (Individual data are given in columns 6 and 7 of Table 2). No natural distinction between small and large MFs and no dichotomy in the standard deviation of MF was observed. Given the median value for variability of 5.3, it seems reasonable to use the criterion value of 6 AMS-points to define the presence of diurnal variation.

3.2. Mood Fluctuation (MF) and Diurnal Variation (DV) measured by self-assessment and by retrospective assessment

The longitudinal records of self-rated mood largely vary between individuals. Two extreme examples of individual mood records are presented in Fig. 1. Fig. 1(top) shows the course of mood of a patient (No. 8 in Table 2) showing hardly any variation within days. Fig. 1(bottom) demonstrates another example, that of patient No. 39 in Table 2. This patient showed mood fluctuations reaching the criterion for positive DV on almost every day during his depressive state.

The other patients showed patterns in between these extremes. Figure 2(top) shows the frequency distribution of the average daily mood fluctuations of the patients. In order to give an impression of the variability of mood fluctuations, the frequency distribution of the standard deviation of the MFs is shown in Fig. 2(bottom). (Individual data are given in columns 6 and 7 of Table 2). No natural distinction between small and large MFs and no dichotomy in the standard deviation of MF was observed. Given the median value for variability of 5.3, it seems reasonable to use the criterion value of 6 AMS-points to define the presence of diurnal variation.

Based on the 6 point difference criterion, the occurrence of DVs has been calculated. In Table 2 patients are ranked on the basis of their individual percentage of positive DVs (Table 2, column 8). Because differences between adjacent patients are small, no clear dichotomy can be observed between patients who had many days with diurnal variations and those who had only a few. In this group of patients, there is only one patient that had predominantly negative diurnal variations (No. 13 in Table 2). This extreme case was excluded for the remainder of the analyses. Averaged over patients, the percentage of positive DVs amounts to 20.8%, negative DVs 6.6% and no DVs 72.6%. No significant correlation (Spearman Rank correlation) was found between age or gender and one of the mood variability measures. The ranges of mood variability measures of the five patients with bipolar disorder show large overlap with the thirty-one with diagnosis of major depression.

The diurnal course of mood is tested against linearity by comparing the linear result of interpolating the values at 9 a.m. and 10 p.m. with the actual depression score at 5 p.m. Due to missing data at 5 p.m., 3514 days were available for this analysis. The average difference between the actual score at 5 p.m. and the result from linear interpolation of morning and evening scores is $-0.07$ points (SD = 4.5, Wilcoxon Matched Pairs signed rank test: NS). If days are selected which fulfil the criteria for positive ($n = 559$) or nega-

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1 Records from all patients are available on request.
tive DVs (n = 201), the calculated scores at 5 p.m. and the actual scores at 5 p.m. are not significantly different either (differences respectively 0.58 ± 7.76, NS; -0.03 ± 7.00, NS). However, on the remaining days that do not reach the criterion of DV (n = 2754), the actual score at 5 p.m. is 0.21 points below the calculated score at 5 p.m. (-0.21 ± 4.5, P < 0.005). This reflects a very small average mood improvement in the afternoon compared to the value expected on the basis of linear interpolation.

According to the retrospective assessment of

Table 2
Patient characteristics, number of days used for DV analysis, average amplitude of mood fluctuation and percentage positive and negative diurnal variation (DV) per patient

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</table>

* Patients are ranked according to percentage positive DV.
diurnal variation in the Hamilton interview, 55% (18 out of 33) of the patients belong to the group of ‘diurnal types’ and 45% (15 out of 33) to the ‘non-diurnal types’. All ‘diurnal patients’ reported to belong to the so called ‘typical diurnal variations’ group with better mood in the evening than in the morning. These groups had a significant difference (Mann-Whitney U-test) in the average mood fluctuation (AMF; diurnal: 3.5 ± 4.7, non-diurnal: 0.4 ± 1.1, \( P < 0.05 \)), the average standard deviation of MF (diurnal: 8.1 ± 5.1, non-diurnal: 4.3 ± 2.3, \( P < 0.05 \)) and the average frequency of positive DVs (diurnal: 26.3 ± 22.1, non-diurnal: 9.9 ± 8.0, \( P < 0.05 \)), but not in the average frequency of negative DVs (diurnal: 7.1 ± 5.7, non-diurnal: 6.5 ± 6.1, NS). Although there are significant differences between the two groups with respect to AMF, the standard deviation of MF and frequency of positive DVs, Fig. 3 indicates that the groups show considerable overlap.

### 3.3. Mood variability in relation to severity of depression

#### A comparison of individuals

In order to assess the severity of depression, the Hamilton rating scale for depression (HRSD) is by far the most frequently employed instrument. It measures severity in terms of an average over a period of days. If in this period of days diurnal mood variations occur, the frequent (daily) moments of relief will influence the ratings of all items in the HRSD. This results in a less severe depression rating. In fact, the severity of depression as rated with the 17 item Hamilton scale (HRSD\(^7\), \( n = 33 \)) was found to correlate negatively with the standard deviation of MF (\( R_s = -0.44, P < 0.05 \)) and with the frequency of positive DVs (\( R_s = -0.39, P < 0.05 \)). The correlations of HRSD\(^7\) with AMF and with frequency of negative DVs did not reach significance (re-

![Fig. 1. Two examples of longitudinal mood registrations in depressed patients obtained by self-ratings on the AMS (Von Zerssen, 1976), three times daily. Each dot represents one self-rating; the ratings of 1 day are joined with a straight line.](image)
respectively: $R_s = -0.30, P = 0.09$; $R_s = -0.20, P = 0.26$). The negative correlations are, in our opinion, rather trivial. The relationship between severity of depression and DV occurrence gains in interest, however, when severity of depression is defined independent of diurnal changes. For this reason the mean depression score (AMS) at 9 am during the first 14 days after admission was calculated for each patient (mean: 43.9 ± 9.1, $n = 38$). No significant correlation was found between this depression measure within 2 weeks after admission and either AMF, the standard deviation of MF or frequency of positive or negative DVs calculated over the entire depressive episode.

A comparison within individuals

Visual inspection of all individual mood records did not reveal any temporal pattern in the occurrence of DV. Periods with DVs were observed in all states of the illness: preceding or during mood improvement, as well as, during persistent depressed states. In some individuals DVs seem to occur at random, in others they occur in distinct bouts.

To examine the possible relationship between the occurrence of DV and mood variability, and the actual severity of depression within individuals, the AMF, the standard deviation of MF and the percentage of positive and negative DVs were calculated for three classes of morning depression scores: between 21 and 30; 31 and 40; and 41 and 50. The choice of 21 as the lowest and 50 as the highest possible value allows for the occur-
Figure 4. Various mood variability measures averaged over days in three classes of morning depression scores. Only patients who contributed for at least 6 days are included (n = 17) in the various bins. (top-left) Average mood fluctuation (AMF); (top-right) standard deviation of mood fluctuation; (bottom-left) frequency of positive diurnal mood variations; (bottom-right) frequency of negative diurnal mood variations.

3.4. Interdependence of various measures of mood variability and response to total sleep deprivation (TSD)

Except for the relationship between AMF and percentage negative DVs, all mood variability measures correlated with each other (Spearman rank correlations, see Table 3). Variability (the standard deviation of MF) shows the highest correlation with all other mood measures mentioned, and interestingly also with TSD response. To obtain a more adequate picture of the interrelatedness of the various variables, partial correlations have been carried out. The correlation between the standard deviation of MF and TSD response remains significant ($r = 0.51$, $P < 0.005$) when corrected for AMF in combination with percentage positive DV and percentage negative DV. The correlation of AMF with TSD response was negative when the contribution of the standard deviation of MF, percentage positive DV and percentage negative DV was partialled.

Table 3
Interrelatedness of various mood measures and their relationship with the response to total sleep deprivation (TSD) (Spearman rank correlations)

<table>
<thead>
<tr>
<th>SD of MF</th>
<th>% pos DV</th>
<th>% neg DV</th>
<th>TSD response after no DV</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 38)</td>
<td>(n = 38)</td>
<td>(n = 38)</td>
<td></td>
</tr>
<tr>
<td>AMF</td>
<td>$R = 0.58$ ***</td>
<td>$R = 0.78$ ***</td>
<td>$R = -0.08$</td>
</tr>
<tr>
<td>SD of MF</td>
<td>-</td>
<td>$R = 0.91$ ***</td>
<td>$R = 0.65$ ***</td>
</tr>
<tr>
<td>% pos DV</td>
<td>-</td>
<td>-</td>
<td>$R = 0.43$ **</td>
</tr>
<tr>
<td>% neg DV</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

For abbreviations see Table 1.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. 

were included in the analysis. The data are presented in Fig. 4. Multivariate analysis of variance with repeated measurements (Wilks's lambda, 3 levels) yielded no significant differences between the three morning-depression score intervals for AMF ($0.71$, $P = 0.07$), the standard deviation of MF ($0.91$, $P = 0.49$), frequency of positive DVs ($0.71$, $P = 0.08$) and frequency of negative DVs ($0.91$, $P = 0.47$). The non-significant trends suggest decreasing mood variability with decreasing severity of depression.
4. Discussion

4.1. Mood variability measured by self-assessment and by retrospective assessment

Diurnal mood variations, recorded on the basis of self-assessments, appear to occur frequently. Averaged over 39 patients, positive DVs were measured on 20.8% of the days while a negative DV has been found on 6.6% of the days. Mood variations below the criterion for DV were observed on the remaining 72.6% of the days. From visual inspection of the longitudinal registrations, it is concluded that DVs occur very irregularly in subjects. The only comparable data set in the literature is the one published by Stallone et al. (1973). These authors reported on the mood scores rated by 10 depressed patients on 643 days. The percentage of positive DVs averaged over the patients was 25.9%, that of negative DVs was 13.6% and that of no DVs was 60.5%. Overall, these results are consistent with those of our study. The small number of negative DVs in our study seems to be the main difference. That they, nevertheless, occur in our group is remarkable because global assessment yielded only subjects who reported ‘typical DVs’ (after 1 subject was removed). The remaining discrepancies between our study and Stallone et al. are probably due to the use of different rating scales and to differences in criteria (Tölle and Goetze, 1987). Unintended selection may, of course, have taken place because the group was a selection of a severely depressed inpatient population.

Inclusion of the 5 p.m. rating in the analysis suggests linearity of the mood course on days with DV. Linear interpolation leads to expected values for the measurement at 5 p.m. that are very close to the actual scores on days which fulfill the criteria for positive or negative DV. On days without large differences between morning and evening depression scores, the actual score at 5 p.m. showed a slightly but significantly lower value (0.21 AMS units) than would be expected on the basis of linear interpolation. Tölle and Goetze (1987) reported numerous patterns of mood variation on days when patients were asked about the course of mood during the preceding 24 hours. The significance of non-linearity or linearity is unclear, but the finding that mood improvement shows a linear course on days with DV affirms the use of morning-evening differences and variance as mood variability measures.

The majority of studies that report on the frequency of DVs are based on a questionnaire or interview applied only once or very few times during the course of depression (Waldmann, 1972; Von Knorring et al., 1977; Graw et al., 1980; Carpenter et al., 1986; Stieglitz et al., 1988). The percentage of patients reporting DVs in these studies varies from 50 to 75%. According to retrospective assessment in our study, 55% of the patients reported DVs, in this case all of them ‘typical DVs’ (i.e., morning lows). However, not all self-defined diurnal patients actually showed DVs in the subsequent recording period, while, on the other hand, some of the self-defined non-diurnal patients did show DVs. Together with the fact that both diurnal and non-diurnal patients occasionally showed negative DVs, the conclusion must be that there is a discrepancy between the results of global retrospective assessment and those of the longitudinal registration of DV of mood. The explanation of a false retrospective perception in depressives has been proposed (Williams et al., 1975). From our study it is conceivable that it is difficult to rate a phenomenon with such an irregular occurrence. An alternative explanation of the discrepancy between the results of retrospective assessment and longitudinal registration might be that the period of reference is different. The interview in our study took place at the beginning of the stay in hospital, while most of the longitudinal data concerns the period
thereafter. However, an interview at the end of the recording period would be inadequate to find discrepancies between retrospective and longitudinal data, because of the emphasis on mood changes by recording mood three times daily over a long period. Contradictory to the ‘forced’ dichotomy of retrospective assessments, no obvious cutting point dividing the group into diurnal and non-diurnal types exists on the basis of the longitudinal records of self-assessments of mood.

4.2. Mood variability and severity of depression

The relationship between the occurrence of DVs and severity of depression can be discussed in two different ways: between subjects and within subjects. **Between subjects** no significant correlations were found between self-rated morning depression at admission and any mood variability measure (AMF, standard deviation of MF or frequency of positive or negative DVs) during the depressive period under study. However, a negative correlation is found between the HRSD-score and mood variability. This result contrasts with the results of Haug and Fähndrich (1990) who did not find a significant correlation. The negative correlation in our data may well result from a methodological cause, as explained previously. Some authors suggest that DVs appear with decreasing severity of depression and disappear when depression becomes more severe (Middelhoff, 1967; Waldmann, 1972). This finding might be caused by the same methodological problem. An alternative possibility is that DVs occur at all levels of severity of depression, but that it is not possible to measure them during severe depression due to limitations of the rating scale (‘ceiling effects’).

The relationship of the severity of depression and the occurrence of mood variability within individuals can only be studied in a longitudinal design. In the present registrations, within the limitations of the applied rating scale, there is no difference in mood variability on days assigned to three levels of morning depression (Fig. 4). From these results it must be concluded that the incidence of DVs does not occur primarily during mood improvement or remission.

4.3. Mood variability and the TSD response; interpretation in terms of regulatory processes

The mood measure which showed the strongest correlation with TSD response was the standard deviation of mood fluctuation ($R = 0.65$). The correlation remained significant when it was corrected for the contribution of AMF, percentage positive DVs and percentage negative DVs. The correlation between percentage positive DVs and TSD response was almost as high ($R = 0.61$), but disappeared when it was corrected for the other mood variability measures. The correlation between AMF and TSD response was only $0.38$. Even the percentage of negative DVs is positively correlated to TSD response. This suggests that the direction of mood fluctuation is not the most important parameter for the response to TSD. Variability of mood, as measured with the standard deviation of MF, seems to be a more powerful predictor of the response to TSD than the frequency of positive DVs or the AMF. This conclusion can, in fact, also be inferred from an earlier study by Reinink et al. (1993). In that study the amplitude of *absolute* MFs and the frequency of *positive plus negative* DVs were the best predictors. These measures are mathematically related to variability. The negative partial correlation of AMF with TSD response remaining after correction for the standard deviation of MF, the percentage of positive DV and the percentage of negative DV is difficult to interpret.

Although this is only based on correlations, it is tempting to interpret these results in a regulatory way. Assuming that external influences are similar for all subjects, large mood variability might be explained by an increased susceptibility to external (and/or internal) stimuli. Examples of these stimuli could be factors related to sleep or to the sleep-wake cycle itself, TSD, and also social events. Thus, patients who are more susceptible to stimuli are more likely to vary in mood and have a higher chance of showing DVs. The origin of this susceptibility is unknown although involvement of the ‘instability of the depressed brain state’ has been suggested (Van den Burg et al., 1992). The hypothesis of increased susceptibility may also explain why DVs are more com-
mon in responders to antidepressive medication (Fahndrich, 1983; Haug and Stieglitz, 1990); medication being yet another kind of stimulus. Similarly it would explain why TSD responses give a good prediction of the therapeutic outcome of antidepressive drug treatment (Wirz-Justice et al., 1979; Fahndrich, 1983). The present analysis suggests that variability of mood as measured by the standard deviation of MF could be an even better predictor.

Two observations are not explained by this reasoning; the fact that positive DVs are more prominent than negative DVs and the fact that the type of diurnality, assessed retrospectively, is crucial to TSD response (Reinink et al., 1990). One explanation for the predominance of positive DVs could be that in most patients mood improves in the course of their stay in the ward, resulting in an average daily mood improvement, which might contribute to a positive AMF and an increased number of positive DVs. However, because diurnal variations do not occur exclusively during improvement, this cannot be the only explanation of the frequency and amplitude of the positive mood fluctuations observed. Another possibility relates to a hypothetical mechanism for the TSD response, proposed by Van den Burg et al. (1992). According to this hypothesis, it is suggested that the antidepressive response to TSD results from a disinhibitory process induced by increased ‘cerebral fatigue’ in the course of wakefulness. Obviously the same disinhibition process could explain the predominance of positive DVs. Arousal mechanisms are also of interest from another point of view. Bouhuys et al. (1989) demonstrated that the clinical response to TSD can be predicted by high levels of arousal, measured with ethological methods. More research on arousal mechanisms of patients with various amounts of mood variability might give clues to the question why positive daily mood variations predominate.

It is not clear how to interpret the relationship between the type of diurnality and the TSD response. Reinink et al (1990) reported that self-defined positive diurnality predicts a good response to TSD while the opposite holds for self-defined negative diurnality. This finding has as yet not been replicated, probably due to the low incidence of patients with self-defined negative diurnality. Riemann et al (1991) reported that patients whose DV was positive prior to TSD responded better than those whose DV was negative or lacking. Global assessments of diurnality are not presented in that study and because of the irregularity of DVs this cannot be deduced from 2 days of mood assessment. As a consequence, the data cannot be used to clarify the relationship between the type of diurnality and TSD response. Whether or not variability is an important variable for TSD response in those subjects with self defined negative diurnality could not be tested in our study, because only one such subject was included in the sample (No. 13). This subject did not participate in a sleep deprivation protocol.

On the basis of our data, theories in which DVs are related to disturbed chronobiological mechanisms (Hall et al., 1964; Fahndrich, 1988) or simply represent an underlying circadian rhythm (Tölle, 1991) cannot be rejected. The facts, however, that in most patients diurnal variations occur irregularly and do not show a persisting 24-hour rhythmicity and mood variability being a better predictor for the sleep deprivation response than the frequency of positive mood variations or the average amplitude of mood fluctuations, do not support such hypotheses. A close link between sleep need ('factor S') and mood, as suggested in the S-deficiency hypothesis (Borbély and Wirz-Justice, 1982), is not very plausible either, because of the large variability of the phenomenon. In our opinion it could be that the susceptibility to stimuli varies between subjects, causing mood swings. The sleep-wake cycle itself or other rhythms driven by the biological clock can be considered in this reasoning as examples of such stimuli.

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