Social Rhythm Regularity Predicts Outcome of Bright Light Therapy in Elderly Patients with Major Depression; Prospective and Predictive Findings from the Randomized Placebo-Controlled Trial.


Submitted
ABSTRACT

Context: Major depressive disorder (MDD) in elderly patients is frequently accompanied by symptoms suggestive of circadian rhythm disturbances, associated with impaired functioning of the suprachiasmatic nucleus, the biological clock of the brain. Endogenously generated circadian rhythms are synchronized with the environment via Zeitgebers, of which daylight and social rhythms are the most important. MDD is associated with low social rhythm regularity, reflecting deteriorating daily life structure. However, it has never been studied whether low social rhythm regularity is therefore predictive for response to bright light treatment.

Objective: To study social rhythm regularity before an effective clinical trial with bright light therapy (BLT) in elderly patients with MDD.

Design, setting, and Participants: Double-blind, placebo-controlled randomized clinical trial in 89 out-patients of 60 years and older with MDD, assessed at baseline (T0), after 3 weeks of treatment (T1) and 3 weeks after the end of treatment (T2).

Intervention: Three weeks of 1 hour early morning BLT (pale blue, 7500lux) v. placebo (dim red light, 50lux).

Main Outcome Measures: Social Rhythm Metric-5 item version (SRM-5) scores before treatment, in which a lower score represents lower regularity. Percentage improvement on the 17 item version of the Hamilton Scale for Depression (HAM-D) at T1.

Results: A lower SRM-5 score at baseline was associated with more clinical improvement on the HAM-D in the BLT group ($r = -.502, P=0.004$), but not at all in the placebo group ($r = .002, P=0.992$). The mean SRM-5 score in the BLT group was lower in responders (4.61; s.d., 1.14) than in nonresponders (5.58; s.d., 0.71; $P=0.008$). At the SRM-5 score cut-off of ≤5, the relative risk (RR) of improvement on the HAM-D of ≥50% was 6.14 (95% CI, 0.94 to 39.81).

Comment: Low baseline SRM-5 scores contribute to the prediction of response on BLT in elderly patients with MDD, suggesting that low social rhythm regularity reflects the need for strong Zeitgebers to successfully entrain the circadian system.

Trial Registration: clinicaltrials.gov Identifier NCT00332670
MAJOR DEPRESSIVE Disorder (MDD) in elderly patients is frequently accompanied by symptoms suggestive of circadian dysfunction, such as altered sleep-wake patterns, diurnal mood variation, energy level, and often, endocrine dysfunction.\textsuperscript{1-3} A deteriorating suprachiasmatic nucleus may contribute to some of these changes.\textsuperscript{4-6} In humans circadian rhythms are largely endogenously generated by the suprachiasmatic nucleus (SCN), and synchronized with the environment via Zeitgebers.\textsuperscript{7} The most important Zeitgeber are daylight and social rhythms. The social environment is able to entrain circadian rhythms, e.g. via exposure to sunlight when going outdoors. Also, non-photic social Zeitgebers like daily activities, mealtimes, or social interactions entrain circadian rhythms.\textsuperscript{8-10} Patients with MDD show low social rhythm regularity, reflecting loss of daily life structure.\textsuperscript{11-15} However, it remains unclear why patients with depression have less regular schedules.\textsuperscript{13} Two hypotheses have been proposed. First, less regularity could reflect that patients with MDD are suffering from more life events and less regular demands from the environment, acting as sources of circadian rhythm disruption (Zeitstörrers). Second, the circadian pacemaker could have lost its synchronizing responsiveness to time cues.\textsuperscript{16-18} Clarification of this issue is considered relevant for the validity of the social Zeitgeber theory, describing how social rhythmicity influences circadian rhythmicity, offering a framework for understanding rhythm disturbances in MDD (see \textbf{Figure 4.1}, p.94).\textsuperscript{13}

However, it has never been studied how bright light treatment (BLT), known as an effective antidepressant\textsuperscript{19} and stimulant of circadian rhythms,\textsuperscript{20} influences social rhythm regularity. Moreover, if impaired social rhythm regularity reflects the need for strong Zeitgebers in order to successfully entrain the circadian system, then it could add to the prediction of treatment response to BLT. In nonseasonal MDD no predictors of response are known. In seasonal affective disorder, however, several predictors have already been described. Oren \textit{et al}\textsuperscript{21} found that hypersomnia, carbohydrate craving and suicidality were positive predictors. Lam \textit{et al}\textsuperscript{22} found correlations for hypersomnia, increased eating and younger age. Krauchi \textit{et al}\textsuperscript{23} found that consuming afternoon and evening carbohydrates, but not diurnal variation or hypersomnia, predicted response. Meesters \textit{et al}\textsuperscript{24} found no predictive value in diurnal variation or hypersomnia. Terman \textit{et al}\textsuperscript{25} found that light-response in seasonal affective disorder is predicted by a dominant atypical symptom profile, and melancholia with nonresponse.

The aim of the present study was...
Fig. 4.1 The Social rhythm theory. Depressive episodes partly arise as a consequence of life events and difficulties, particularly those involving separation or loss disrupting social Zeitgebers (external cues that function to entrain biological rhythms). Disturbed social rhythms, in turn, derail circadian rhythms. Moreover, disrupted circadian rhythms, due to abnormal hypothalamic pacemaker functioning, may contribute to social rhythm disturbances. Ultimately, it is postulated that chronic disruptions of social and biological rhythms together contribute to the vulnerability for MDD. In this scheme a protective pathway is added. Using bright light therapy the hypothalamic circadian pacemaker is stimulated, which protects against social rhythm disruption and decreases circadian rhythm disruption symptoms and ultimately depressive symptoms.

to investigate social rhythms during an effective randomized clinical trial with BLT in elderly patients with nonseasonal MDD. In order to answer the questions whether low social rhythm regularity would contribute to the prediction of treatment response with BLT. Secondly the present study aims to describe how

BLT changes social rhythm regularity during the course of clinical recovery from depression?
METHODS

The current study was executed in accordance with the Helsinki Declaration. Approvals were obtained from the Dutch authorities and the medical ethical committee (METIGG [Medisch-ethische Toetsingscommissie Instellingen Geestelijke Gezondheidszorg], Utrecht). Trial design, participants, intervention details, primary efficacy outcome analysis, cortisol, sleep and melatonin data from this trial have been published in a separate paper.

STUDY DESIGN

We used a randomized, double-blind, placebo-controlled design to compare the antidepressive effects of BLT and placebo. Permuted block randomization in subsets of 10 was performed, with separate randomizations for the strata of patients who used antidepressants (AD+) and those that did not (AD-). The two randomization lists, prepared by an independent researcher (B.M.J.U.) not involved in the recruitment and using a computer-generated table, were transferred to a sequence of sealed opaque envelopes.

Study patients were informed that the primary goal of the study was to investigate spectrum-dependent efficacy differences between blue and red. Investigators were blinded to the condition because the lamps were delivered at the patients’ homes by protocol-blinded instructors, who were also informed that the study aimed for spectrum-dependent efficacy differences. Patients were asked not to discuss any details of their condition with the interviewers. In 2 cases, patients did reveal their assignment, after which the interviewer was replaced.

STUDY INTERVENTION

Patients were randomly assigned to receive bright pale blue or dim red light treatment therapy at home using 2 light boxes (Philips Bright Light Energy HF 3304; Koninklijke Philips Electronics NV, Eindhoven, the Netherlands). Concealed within the light boxes, a single-layer filter was wrapped around the fluorescent tubes: a mist-blue filter (Model 061; Lee Filters, Andover, England) with high-throughput pale blue (7500 lux) for the active condition and a blood-red filter (Model 789; Lee Filters) with low throughput red (50 lux) for the placebo condition. Dim red light can be considered to be biologically inactive.

Given the proposed interaction between exposure intensity and duration for the efficacy of BLT, we chose an exposure of 60 minutes in the early morning at about 7500 lux. For BLT of nonseasonal MDD in elderly patients, there is no consensus with respect to optimal
timing, dosage and treatment duration. We chose 3 weeks of daily light exposure, because most studies thus far used short term treatment of up to 1 week,\textsuperscript{29-42} and because the Cochrane review on BLT in nonseasonal MDD concluded that BLT may be effective in as little as 1 week.\textsuperscript{43}

OUTCOME MEASURES

Social rhythm regularity The social rhythm metric (SRM-5) is a diary-like questionnaire that quantifies the extent to which a person’s life is regular vs. irregular on a daily basis with respect to event timing.\textsuperscript{44} The SRM-5 has 5 specified events, and it requires the subject to record daily details of the time of day each event occurred. The event is considered to be a hit if it falls within 45 minutes of its predicted habitual time. If an event has more than 3 hits per week, it is used to derive a score of 0-7 for the week involved. Data for each week are analyzed as a unit. The SRM-5 score thus lies on a continuum between 0 and 7, with 0 representing lowest irregularity and 7 highest regularity. Further details on the scoring algorithm are given in Monk \textit{et al.}\textsuperscript{12} The SRM-5 has a moderate to high test retest reliability. Monk \textit{et al}\textsuperscript{11} reports a high significant correlation (rho=0.44; \( P < 0.001 \)) between week 1 and 2. The SRM-5 has been described as a valid instrument in different studies.\textsuperscript{11}

The SRM-5 not only measures the rhythmicity of the events, but its Activity Level Index (ALI) also measures the volume of activities. The ALI is simply a count of the number of performed categories regardless of how regularly they are performed.\textsuperscript{12} The ALI score ranges from 0 to 35 (5 event times in 7 days).

PROCEDURE

Included patients completed 1 week of SRM-5 before therapy started (T0) and were asked to keep up the diary during treatment and after treatment. SRM-5 scores from the third week of treatment were reflecting T1, and scores from the third week after treatment were reflecting T2.

STATISTICAL ANALYSES

Baseline characteristics were compared using two-sided \( t \)-tests for continuous data and \( \chi^2 \)-statistics and two-tailed Fisher exact tests for categorical data using SPSS 17.0 software (SPSS Inc, Chicago, USA) (Table 4.1, p. 98). The assumptions of linearity, normal distribution of residuals and consistent variance of residuals were tested and found to be satisfactory for all analyses. All significance levels were set at \( P < 0.05 \) with 2-sided testing. Means and 95\% confidence intervals (CIs) are provided if appropriate.

The primary analysis comprised an analysis of the predictive value of SRM-5 scores at baseline on the percentage
improvement on the HAM-D score. The relation between SRM-5 and clinical improvement between T0 and T1 separate regression analyses were performed using percentage improvement on the HAM-D score as dependent and SRM-5 scores at baseline as independent variables. The correlation between SRM-5 and treatment response, defined as ≥50% treatment response on the HAM-D, was also studied using Spearman’s correlations. Effect size Cohen’s d was calculated.

To study the predictive value of SRM-5 scores on treatment response logistic regression analysis was performed.

Finally SRM-5 scores were digotomized using a cut-off value of ≤5, which was chosen because it reflects the mean SRM-5 score at baseline. We determined its relative risk on treatment response, defined as ≥50% decrease in HAM-D scores.

Ancillary analyses comprised Spearman’s correlations between baseline and posttreatment HAM-D scores, as well as for the atypical balance score, defined as 100* [8 item atypical score] / [SIGH-SAD total]), which has been shown to possess predictive power in patients with seasonal affective disorder.25

The secondary analysis comprised an analysis of the treatment effects of BLT on SRM-5. Treatment effect analyses fulfil intention-to-treat (ITT) criteria since none of the participants assigned to one condition switched to another, and analyses involved all observations of all participants until study end or withdrawal. As sensitivity analysis both a baseline carried forward as well as a completers analysis was performed. Where not otherwise indicated, data are expressed as mean (s.d.).

RESULTS

GENERAL

We included and randomized 89 patients, with 42 allocated to the BLT condition and 47 to the placebo condition. Baseline depression characteristics have been published elsewhere.45 There were no hospitalizations or suicides or other deaths. Randomization was balanced with respect to demographic and comorbidity characteristics and psychiatric comorbid diagnoses (Table 4.1, p. 98). Groups were not balanced with regard to Mini-Mental State Examination score (MMSE score; mean placebo group score, 28.5 [s.d., 1.8]; mean BLT groups score, 27.6 [2.0]; P=0.04), and to the pre-treatment HAM-D score (mean placebo group score 16.0 [4.7]; BLT group score 18.4 [5.6]; P=0.03).

In total, 89 patients completed 418 valid SRM-5 diaries. At T0 67 patients had complete SRM-5 measurements. The mean SRM-5 score for all patients was 5.0 (1.0). At T1 61 patients and at T2 50 patients had complete SRM-5 scores.

97
Table 4.1 Demographic characteristics of all randomized study participants (n=89) by assignment (BLT vs. Placebo)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=47)</th>
<th>BLT (n=42)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (s.d.), y</td>
<td>69.00 (6.6)</td>
<td>69.67 (8.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Sex (female/male) (%F)</td>
<td>30/17 (63%)</td>
<td>28/14 (66.7%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Partner, N (%)</td>
<td>18 (38.3%)</td>
<td>16 (38.1%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Body height (m), mean (s.d.)</td>
<td>1.69 (0.08)</td>
<td>1.68 (0.07)</td>
<td>0.55</td>
</tr>
<tr>
<td>Body weight (kg), mean (s.d.)</td>
<td>76.37 (14.2)</td>
<td>73.88 (15.1)</td>
<td>0.45</td>
</tr>
<tr>
<td>Body Mass Index(^b) kg/m(^2), mean (s.d.)</td>
<td>26.79 (4.6)</td>
<td>26.15 (4.6)</td>
<td>0.54</td>
</tr>
<tr>
<td>MMSE, mean (s.d.)</td>
<td>28.47 (1.8)</td>
<td>27.60 (2.0)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Abbreviations: MMSE, Mini-Mental State Examination.\(^{53}\)

\(^a\) For comparisons of BLT and control, using t tests (continuous variables) or \(\chi^2\) tests (discrete variables).

\(^b\) Calculated as weight in kilograms divided by height in meters squared. Statistically significant test values are depicted in bold font.

Table 4.2 SRM-5 scores

<table>
<thead>
<tr>
<th>Social Rhythm Metric score</th>
<th>Placebo</th>
<th>BLT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>4.82 ± 1.02 (n=36)</td>
<td>5.11 ± 1.05 (n=31)</td>
<td>0.25</td>
</tr>
<tr>
<td>T1</td>
<td>5.40 ± 0.93 (n=27)</td>
<td>4.84 ± 1.24 (n=29)</td>
<td>0.043*</td>
</tr>
<tr>
<td>T2</td>
<td>5.05 ± 1.00 (n=24)</td>
<td>4.70 ± 0.88 (n=22)</td>
<td>0.21</td>
</tr>
<tr>
<td>∆ T0-T1</td>
<td>0.56 ± 0.97 (n=27)</td>
<td>-0.35 ± 1.40 (n=25)</td>
<td>0.008**</td>
</tr>
<tr>
<td>∆ T0-T2</td>
<td>0.19±0.98 (n=23)</td>
<td>-0.67 ± 0.88 (n=23)</td>
<td>0.007**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Activity Level Index</th>
<th>Placebo</th>
<th>BLT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>31.95 ± 3.27 (n=36)</td>
<td>32.79 ± 2.76 (n=31)</td>
<td>0.27</td>
</tr>
<tr>
<td>T1</td>
<td>31.47 ± 3.84 (n=28)</td>
<td>32.80 ± 2.84 (n=29)</td>
<td>0.18</td>
</tr>
<tr>
<td>T2</td>
<td>32.67 ± 3.36 (n=24)</td>
<td>32.68 ± 2.93 (n=22)</td>
<td>0.99</td>
</tr>
<tr>
<td>∆ T0-T1</td>
<td>-0.27 ± 4.16 (n=27)</td>
<td>-0.02 ± 3.49 (n=25)</td>
<td>0.82</td>
</tr>
<tr>
<td>∆ T0-T2</td>
<td>0.66 ± 3.34 (n=23)</td>
<td>0.76 ± 3.26 (n=17)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Abbreviations: BLT, Bright Light Treatment; ∆ change between.

\(*\), \(P \leq 0.05\); \(**\), \(P \leq 0.01\).
SRM-5 and HAM-D scores were neither significantly correlated ($r=0.05; P=0.663$) at T0, not at T1 ($r=0.031; P=0.811$) or at T2 ($r=0.263; P=0.078$).

SRM-5 AND RESPONSE ON DEPRESSION

SRM-5 scores in the BLT group at baseline were significantly inversely correlated with percentage improvement on the HAM-D at T1 ($r=-0.502, P=0.004$), but not in the placebo group ($r=0.002, P=0.992$) (Figure 4.3, p. 100). At T2 we found no correlation between percentage improvement on the HAM-D and SRM-5 scores at baseline in the BLT group ($r=-0.320; P=0.079$).

When treatment response was defined as ≥50% decrease in HAM-D scores at T1, the treatment responder mean baseline SRM-5 score was 4.61 (1.14) and the treatment nonresponder mean baseline SRM-5 score was 5.58 (0.71), the difference being 0.97 (95% CI, 0.3 to 1.7; $P=0.008$). Effect size $r = 0.46$ and Cohen’s $d = 1.02$. To further examine the relation between SRM-5 and clinical improvement separate regression analyses were performed using percentage improvement on the HAM-D score as dependent and

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**Fig. 4.2** Mean Social Rhythm Metric-5 (SRM-5) scores (B) and Activity Level Index (ALI) scores (A) before treatment (T0), in the last week of treatment (T1) and in the third week after treatment (T2).

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SRM-5 scores at baseline as independent variables ($b = -.502, P=0.004$ and $R^2 = 0.252$). Logistic regression analysis was performed for predicting treatment response, defined as $\geq 50\%$ decrease in HAM-D), and was found to be significant ($\chi^2 = 35.241$, d.f. 1, N=40, Nagelkerke $R^2 = 0.293$; $B=-1.186$; s.e.=0.523; $P=0.02$; $b= 0.306$ [95\% CI, 0.110-0.851]). If SRM-5 score was dichotomised using SRM-5=5 as the cut-off score and tested on treatment response defined as $\geq 50\%$ decrease in HAM-D, $\chi^2(1) = 8.330; P=0.004$, with a relative risk for treatment response $RR = 6.14$ (95\% CI, 0.94 to 39.81).

To account for imbalance in baseline MMSE scores, and the possible effects of partnership separate regression analyses were performed adding MMSE ($B=3.831$ [s.e., 2.61], $P=0.154$) and partnership ($B=1.084$ [s.e., 7.779], $P=0.891$).

**ANCILLARY ANALYSIS OF PREDICTORS**

The severity of depression at baseline did not correlate with treatment response ($r=.104; P=0.524$). To draw correspondence with previous studies, we compared Spearman's correlations between baseline and posttreatment HAM-D scores. For raw

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**Fig. 4.3** Scatterplot of the relation between the baseline social rhythm metric-5 score with the percentage improvement on the Hamilton Depression Rating Scale (HAM-D) at T1 (left) and at T2 (right).
scores pre- and posttreatment HAM-D scores showed a significant positive correlation at T1 (r=.619; P=<0.001) and at T2 (r=.658; P<0.001). HAM-D scores at baseline did not correlate with treatment response (percentage baseline) at T1 (r=.104; P=0.525) or at T2 (r=.303; P=0.072).

Also, the Atypical Balance Score (100* [8-item atypical score] / [SIGH-SAD total]) was not correlated with treatment response (r=.129; P=0.426).

EFFECTS OF TREATMENT ON SRM-5

Table 4.2 (p. 98) and Figure 4.3 (p. 100). At baseline, there were no statistically significant group differences with respect to mean SRM-5 score using BLT (5.11 [1.05]) v. placebo (4.82 [1.02]; P=0.25) or with respect to ALI score using BLT (32.79 [2.76]) v. placebo (31.95 [3.28]; P=0.27). In intention-to-treat analysis, between T0 and T1 SRM-5 did not changed significantly from baseline in the BLT condition (-0.35±1.40 points [95% CI, -0.9-0.2]), whereas in patients in the placebo condition SRM-5 scores increased (+0.56±0.98 points [95% CI, 0.2-0.9]), the difference being 0.92 points (95% CI, 0.3-1.6; F 1,30 =7.513; two-sided P=0.008).

Between T0 and T2 (after treatment discontinuation) SRM-5 scores were significantly lowered using BLT (0.67[0.88 points [95% CI, 0.25-1.09]), but unchanged in the placebo condition (0.19 [0.98] points [95% CI, -0.21-0.59]), the difference being 0.86 points (95% CI, 0.25-1.45), repeated measures ANOVA, F 1,33 =3.761; P=0.038). When MMSE, HAM-D scores and living with a partner were used as covariates (F 1,30 =3.371) P=0.049. As sensitivity analyses, both BCF and CA showed comparable results. The BCF repeated measures ANOVA showed F 2,69 =4.358; P=0.015, and using MMSE, partnership and baseline HAM-D scores as covariates, F 2,66 =3.266; P=0.044. The CA repeated measures ANOVA showed F 2,30 =4.258; P=0.024, and using MMSE, partnership and baseline HAM-D scores as covariates, F 2,28 =3.371; P=0.049.

COMMENTS

The main finding of the present study is that lower social rhythm regularity in elderly patients with nonseasonal MDD contributes to the prediction of treatment response to BLT, but not to placebo (Figure 4.3, p. 100). We did not find other factors associated with BLT effectiveness. Especially, we did not find the atypical symptoms, such as hypersomnia, afternoon or evening slump, reverse diurnal variation (evenings worse), carbohydrate craving to predict response, as Terman et al did in patients with SAD.25 Our findings are in line with the findings by Terman et al that social withdrawal, resulting in decreased social rhythm regularity, was a negative predictor of improvement with small-to-moderate
effect size\textsuperscript{25}

Our finding is of potential clinical relevance and supports the social Zeitgeber/Zeistörer theory\textsuperscript{46, 47} postulating that social rhythm disruptions precede circadian rhythm disruptions in vulnerable individuals (Figure 4.1, p. 94). Ever since Ehler’s social Zeitgeber theory was published in 1988\textsuperscript{10} considerable research and programs have been developed to regularize social rhythms in patients with mood disorders. In bipolar disorder the concept gave rise to the Interpersonal and Social Rhythm Therapy (IPSRT).\textsuperscript{48} Prigerson \textit{et al}\textsuperscript{18} suggested that the preservation of intact social rhythms could serve to protect individuals from bereavement-induced depression. Monk \textit{et al}\textsuperscript{16} showed that social rhythm regularity, in healthy individuals, appears to increase over the life span and hypothesized that this represents an adaptation to age-related changes in the circadian system’s sensitivity to entraining agents. Moreover, high SRM-5 scores, reflecting high social rhythm regularity, have been found in extremely well-adjusted and healthy octogenarians.\textsuperscript{49}

In the present study in elderly patients with nonseasonal MDD, BLT induced clinical recovery and was associated with a decrease of social rhythm regularity, without changing the volume of activity, i.e. ALI-scores. In another study it was shown that SRM-5 scores of recovered patients with depression appeared to be similarly to that of controls and mainly driven by the involvement of significant others. SRM-5 scores of events done alone were lower than those with active participation of others.\textsuperscript{50} Thus, elderly patients with nonseasonal MDD appeared to be ‘borrowing’ their rhythmicity from others.\textsuperscript{47} As BLT is the strongest Zeitgeber, we hypothesize that patients with remitted depression tolerate lower social rhythm regularity (i.e. lower SRM-5 scores) more, with increased ‘social flexibility’ as a consequence. In other words, we hypothesize that BLT ‘overrules’ the social rhythm regularity. This explanation follows Monk and Kupfer,\textsuperscript{51, 52} who suggested that in advancing age the circadian system is failing in the transduction of the endogenous circadian timing system of the hypothalamic suprachiasmatic nucleus to rhythms downstream.

Several limitations should be discussed. At baseline, there was a slight, but statistically significant randomization imbalance for MMSE scores, indicating that BLT allocated patients had slightly lower MMSE scores than placebo allocated patients (Table 4.1, p. 98). In an earlier study by our group it was shown that BLT has beneficial effects on cognition in demented elderly residents of group care facilities.\textsuperscript{20} However, in the present study MMSE scores were well above cut-off scores for cognitive impairments. In our regression analyses we did not find MMSE to have
influenced the results. Further, we did not measure bereavement or other life events, which would allow analysing the pathway between life events and social Zeitgeber changes. Also, there is evidence that the social component itself is of fundamental importance, because social activities involve participation in a larger community, and are often, but not always done with other people. However, the present study involves non-institutionalized elderly patients, both living alone and living with somebody, there was no randomization imbalance with respect to partnership, and partnership was of no influence on HAM-D outcome or SRM-5 outcomes.

Taken together, the present study indicates that low social rhythm regularity could contribute to the prediction of treatment response to BLT.

REFERENCES

13. Grandin LD, Alloy LB, Abramson LY. The social zeitgeber theory, circadian rhythms, and mood disorders: review


48. Frank E, Kupfer DJ, Thase ME, et al. Two-year outcomes for
interpersonal and social rhythm therapy in individuals with bipolar I disorder. Arch Gen Psychiatry. Sep 2005;62(9):996-1004.


