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Evening preference and poor sleep independently affect attentional-executive functions in patients with depression

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ABSTRACT

Cognitive impairments are well documented in major depressive disorder (MDD), however, they cannot be fully explained by depressive symptom severity. We investigated how diurnal preference and sleep quality affect cognitive function in MDD. In 34 inpatients with current MDD and 29 healthy controls (HC), we obtained diurnal preference (Morningness-Eveningness Questionnaire, MEQ) and subjective sleep quality (Pittsburgh Sleep Quality Index, PSQI). Further, current mood and neuropsychological performance (Trail Making Test, TMT, part A and B) were assessed in the evening and in the following morning. Patients with MDD performed worse than HC on the TMT-B (particularly requiring executive function), but not on the TMT-A (assessing foremost visuomotor processing speed). In general, participants with evening preference (MEQ-score median split) performed poorer on the TMT than participants with morning preference. Subgroup analyses within MDD confirmed the negative effect of evening preference on the TMT. In addition, patients with severely impaired sleep quality (PSQI $>$ 10) performed cognitively worse than patients with normal to moderately impaired sleep quality (PSQI $\leq$ 10). The results were largely independent of current mood state. Our findings suggest that evening preference and severely impaired sleep quality independently contribute to cognitive impairment in MDD.

1. Introduction

Major depressive disorder (MDD) is a disabling psychiatric condition that has been associated with impairments in various cognitive domains, particularly in executive functions (Snyder, 2013). Cognitive impairments in MDD are not only particularly disabling as reported by patients, they also deserve clinical notice since they are associated with poor response to pharmacotherapy (Groves et al., 2018) and psychosocial dysfunction (Cambridge et al., 2018).

The relationship between cognitive performance and depression severity is often found to be small or insignificant (e.g. Albert et al., 2018) which does not support the idea that cognitive deficits occur only secondary to the affective symptoms in MDD. Moreover, cognitive impairments often persist after clinical recovery (Reppermund et al., 2009) and were even found in healthy adults with a high familial risk of mood disorders (Papmeier et al., 2015). Several clinical variables have been associated with increased cognitive impairments in MDD, including subtypes with melancholic symptoms (Michopoulos et al., 2008) or severely impaired sleep quality (Kundermann et al., 2016).

This raises the question whether cognitive impairment in MDD reflects, at least partially, a more trait-like feature of depression related to other premorbid factors. The majority of studies addressing factors contributing to cognitive impairment in MDD focused on clinical features of MDD but not on premorbid traits. An interesting candidate variable could be the irregularities of circadian rhythms and sleep which are frequently observed in MDD, not only during acute episodes, but partially also in prodromal and remission states (Srinivasan et al., 2009). Circadian rhythms are behaviorally expressed by preferred sleep-waking and activity times which considerably vary across individuals – referring to an individual's diurnal preference – on a

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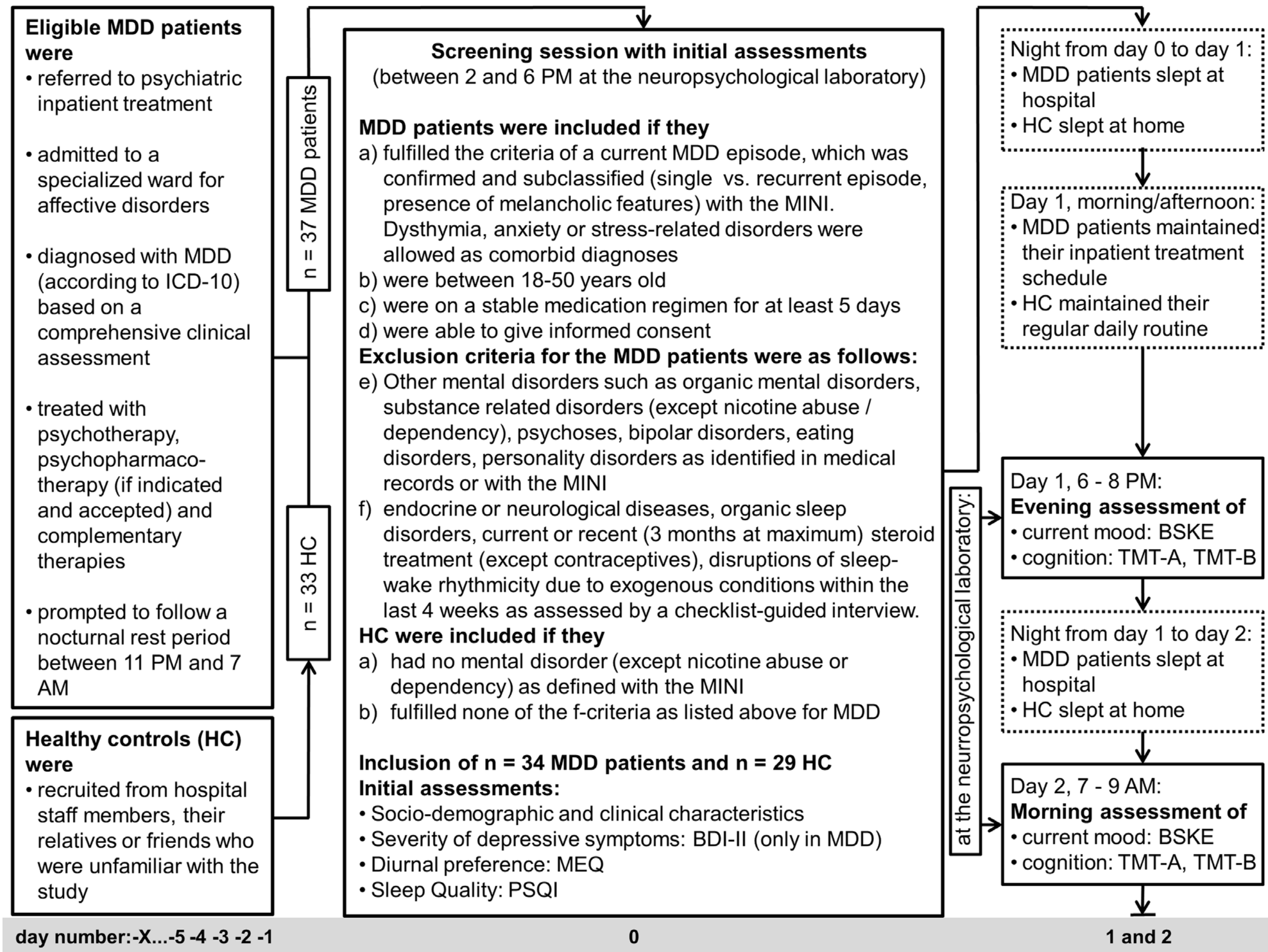

Fig. 1. Recruitment of patients with major depressive disorder (MDD) and healthy controls (HC), inclusion procedures and time schedule of measurements.

continuum from strong morning preference to strong evening preference (i.e. an individual's chronotype). The individual diurnal preference seems to be a trait-like characteristic with substantial heritability (Von Schantz, 2017).

There is growing evidence that evening preference is associated with an increased risk for MDD and for various other mental symptoms or disorders such as poor sleep, anxiety, bipolar and seasonal affective disorder (Müller and Haag, 2018). In MDD, studies indicate that evening preference is associated with certain psychopathological features such as more pronounced paranoid symptoms (Gaspar-Barba et al., 2009), insomnia (Chan et al., 2014) or increased depressive thinking such as self-depreciation or pessimism (Müller et al., 2016). To our knowledge, previous studies did not examine the influence of diurnal preference on cognitive impairment in MDD. However, the hypothesis that diurnal preference is associated with cognitive impairment in MDD can be derived indirectly: on the one hand, studies describe an association between evening preference and psychotic symptoms, as well as sleep disturbances. On the other hand, these clinical features were found to be correlated with cognitive impairment. Moreover, a few studies showed an association of diurnal preference with cognitive deficits in other diseases: e.g. patients with delayed sleep-wake phase disorder, a clinical variant of extreme evening preference, showed attention impairment, especially in the morning and under forced early awakening (Solheim et al., 2018). Further evidence can be derived from studies in healthy individuals. Kang et al. (2015) reported that evening preference was not only associated with certain personality traits such as impulsivity and sensation seeking, but also with worse response inhibition in a Go/No-Go task. When considering the time of testing in relation to diurnal preference, it was demonstrated that participants with evening preference performed poorer on an attentional control task during early day times than morning oriented individuals while the opposite direction was observed during later daytimes (e.g. Matchock and Mordkoff, 2009), a finding that supports the so-called synchrony effect. However, there are also contradictory findings showing that evening-oriented individuals performed cognitively better on measures of processing speed and working memory, even when tested at their non-preferred time of day (Roberts and Kyllonen, 1999; Schmidt et al., 2015). Summarizing studies in healthy subjects, the relationship between diurnal preference and cognitive performance remains somewhat inconsistent. This is probably due to the methodological heterogeneity with regard to times of testing and neuropsychological tasks which measure specific cognitive abilities (e.g. attention or executive functions), that might be differentially affected by the circadian system and diurnal preference (Schmidt et al., 2007). A major limitation of the aforementioned studies is that they did not systematically incorporated variables such as sleep quality or current mood which may explain performance differences as well (Gobin et al., 2015). Poor sleep quality as well as diurnal variations of mood – typically experienced as mood being worse upon waking and better in the evening (Murray, 2007) – are central features in MDD, both reflecting abnormalities in circadian rhythms. Therefore, these variables as well as daytime preference may contribute to cognitive impairment in MDD.

The present study aimed to investigate the association between self-reported diurnal preference, sleep quality and current mood state with cognitive performance on tasks of attentional-executive functioning in inpatients with MDD and healthy controls (HC). We hypothesized that patients with MDD would exhibit poorer cognitive performance than HC, especially on measures of executive functioning. We further hypothesized that MDD patients with severely impaired sleep quality would show more pronounced cognitive deficits than MDD patients with normal or up to moderately impaired sleep quality, independent of diurnal preference.

2. Methods

This study was part of a larger research project (Sleep, circadian rhythmicity, mood and pain perception in patients with affective and affect regulation disorders and healthy controls) and was approved by the medical ethics committee of the Justus-Liebig-University of Giessen, Germany. The study is registered in the German Clinical Trials Register (DRKS00010215).

2.1. Study sample and design

Inpatients with a current episode of a major depressive disorder (MDD) according to the ICD-10 criteria and healthy controls (HC) were enrolled into the study after giving written informed consent. All participants were recruited between October 2015 and September 2017.

Patients were recruited from consecutive referrals for inpatient treatment. HC were recruited from hospital staff members, their relatives or friends. MDD inpatients and HC were informed about the study and, if interested to participate, invited to a screening session (Fig. 1). In the MDD group, the interval between hospital admission and the screening ranged between 6 and 37 days. 37 MDD patients and 33 potential HC responded to the invitation. All participants were assessed with the MINI Neuropsychiatric Interview (Ackenheil et al., 1999) and a checklist of exclusion criteria. Of these, $n = 7$ could not be included due to the following reasons: acute suicidality requiring change of psychopharmacological treatment ($n = 1$ MDD patient), report of an organic sleep disorder or an endocrine disease ($n = 2$ HC) and $n = 4$ who did not consent to study participation. Immediately after inclusion in the study, MDD patients ($n = 34$) and HC ($n = 29$), initial assessments were conducted. On the subsequent two days, MDD patients and HC underwent an evening testing session regarding current mood and cognitive performance on day 1, which was repeated on the following morning (Fig. 1).

2.2. Measures

2.2.1. Diurnal preference

Diurnal preference was assessed with the German version of the Morningness-Eveningness Questionnaire (MEQ). Adequate reliability (test-retest reliability of $r = 0.965$, $p < 0.0001$) and validity (e.g. correlation with the onset of nocturnally elevated melatonin synthesis of $r = -0.606$, $p < 0.0001$) have been demonstrated previously (Griefahn et al., 2001). The total score is commonly used to classify individuals categorically as evening (16–41), intermediate (42–58) or morning types (59–86). Instead of this classification, we divided the whole sample by using a median split of the MEQ score, which provided the benefit of a larger subgroup sample size.

2.2.2. Sleep quality and sleep times

The German version of the Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire on sleep quality during the last two weeks (Riemann and Backhaus, 1996), which has proven reliability (e.g. internal consistency by Cronbach's alpha of 0.75) and validity in German samples (Hinz et al., 2017). For subgroup analysis, we divided MDD patients into two groups according to the PSQI total score of ≤ 10 (at maximum moderate impaired sleep quality) vs. PSQI > 10 (severely impaired sleep quality, Hinz et al., 2017). Furthermore, participants completed a sleep diary which included their times of going to bed and arising.

2.2.3. Neuropsychological functioning

Visuomotor processing speed was evaluated with the Trail Making Test part A (TMT-A), and executive functioning through the TMT-B (Reitan, 1992). The TMT-A requires connecting 25 circles labeled with numbers in ascending order. In the TMT-B, numbers and letters have to be connected alternately. Participants are asked to connect the circles as fast and accurately as possible. The completion times were converted to age-adjusted *z*-scores (with higher *z*-scores indicating better performance) according to published normative values (Tombaugh, 2004).

2.2.4. Severity of depressive symptoms and current mood

Depression severity was assessed with the Beck Depression Inventory (BDI-II, Hautzinger et al., 2009). Current mood was assessed with a short version (14-items) of the multidimensional mood-states questionnaire (BSKE), which is validated in several German-speaking countries and especially suited for repeated measurements within several minutes to hours (Janke and Debus, 1978). The items consists of nouns and adjectives that describe various positive and negative mood states (example: ‘feeling of fatigue, e.g. tired, sleepy’) which have to be rated on a seven-point scale from 0 (= not at all) to 6 (= very strong). One composite score of current mood was calculated for each participant based on the mean of each positive and each negative (inversely converted) mood item (i.e. higher scores indicate better mood). Current mood was assessed always directly before cognitive assessment.

2.2.5. Socio-demographical and clinical characteristics

Age, sex and years of education were recorded. For MDD patients, diagnoses (including different subtypes such as single vs. recurrent episode, presence of melancholic features) and current medication were noted.

2.3. Statistical analysis

R software version 3.1.2 was used for statistics. Descriptive statistics are given as frequencies and mean ± standard deviation (in figures: ± standard error of mean, SEM). χ^2-analyses were performed for analyzing categorical data (sex, group allocation according to diurnal preference and severity of poor sleep quality). Group comparisons for continuous variables were conducted either with t-tests for independent samples (age, education, diurnal preference sleep quality and bedtimes) or – for those variables measured repeatedly at different day times (cognitive performance and current mood) – using analyses of variance (ANOVA) for repeated measurements with the within-subject factor “time” and the between-subject factors “group” (MDD vs. HC) and “diurnal preference” (morning vs. evening preference). For subgroup analyses within the MDD group, the between-subject factor “sleep quality” (no to moderate vs. severe impairment) was included. To deal with confounding variables, analysis of covariance (ANCOVA) was applied. Pearson's r or point-biserial correlations (r_{pbis}) were calculated to examine relationships between socio-demographical variables, cognitive performance, severity of depression and current mood state (separately for the different times of assessment). The significance level was set at $\alpha < 0.05$. For hypothesis-driven tests with multiple comparisons, Bonferonni correction was used within the category of neuropsychological measures to control type I error.

3. Results

3.1. Study sample

Table 1 lists socio-demographic and clinical characteristics of the sample. Both groups were comparable regarding sex, age, education, diurnal preference and bedtimes (day 1 to day 2). Sleep quality was significantly poorer in MDD patients.

Table 1
Socio-demographical and clinical characteristics of patients with major depressive disorder (MDD) and healthy controls (HC).

Measures	Descriptive statistics MDD (n = 34)	HC (n = 29)	Inferential statistics χ^2/t	p
Sex [female/male]	16/18	16/13	0.412	0.521
Age [years]	33.0 ± 8.9	31.5 ± 7.8	0.710	0.480
Education [years]	11.3 ± 2.3	12.1 ± 3.1	−1.275	0.207
Diurnal preference [MEQ-score]	50.1 ± 11.0	53.5 ± 10.3	−1.264	0.11
Evening type/Neutral type/Morning type [n]	7/21/6	5/14/10	2.351	0.309
Median-Split: MEQ <53/MEQ ≥53 [n]	**18/16**	**13/16**	**0.412**	**0.521**
Sleep quality [PSQI]	10.1 ± 4.2	3.8 ± 1.9	7.270	<0.001
Sleep diary				
Day 1: time of going to bed [hh:mm, PM]	**10:50 ± 1:06**	**11:15 ± 1:20**	**−1.378**	**0.173**
Day 2: time of arising [hh:mm, AM]	**06:32 ± 0:37**	**06:24 ± 0:46**	**0.685**	**0.496**
Severity of depressive symptoms [BDI-II]	28.9 ± 11.6			
ICD-10 main diagnoses				
Type of MDD: single/recurrent	27/7			
Comorbid diagnoses [none/anxiety disorders]	25/9			
Psychopharmacological treatment [no/yes]	8/26			
-SSRI[a] only [n]	10			
-SSRI + *a* low potent neuroleptic [n]	4			
-SSRI + tetracyclic antidepressant [n]	1			
-SSRI + agomelatine [n]	1			
-SSRI + an atypical antipsychotic [n]	1			
-SNRI[b] only [n]	2			
-SNRI + *a* low potent neuroleptic [n]	2			
-SNRI + *a* tricyclic antidepressant [n]	1			
-Agomelatine only [n]	3			
-Mood stabilizer only [n]	1			

[a] selective serotonin reuptake inhibitor.
[b] serotonin and noradrenalin reuptake inhibitor.

3.2. Attentional-executive functioning and current mood: comparison between patients with MDD and HC grouped by diurnal preference

MDD patients and HC were grouped by diurnal preference based on a median split of the MEQ score and labeled as evening preference (MEQ < 53) and morning preference (MEQ ≥ 53), respectively. A higher proportion of males was found in the evening preference group (64.5%) compared to the morning preference group (34.4%; $\chi^2 = 5.723$, $p = 0.017$). Furthermore, years of education were significantly lower in the evening preference group (10.9 ± 2.2 vs. 12.4 ± 3.0; $t = -2.261$, $p = 0.027$).

Fig. 2 shows the descriptive statistics for the TMT at the evening and the morning test session. Since education and sex ($f = 0$, $m = 1$) were neither significantly correlated with TMT-A nor with TMT-B performance (all r between -0.1 and 0.2, all r_{pbis} between -0.250 and -0.1, p values >0.05), both variables were not considered as covariates in subsequent analyses. HC performed significantly better than MDD patients in the TMT-B as indicated by an ANOVA main effect of group ($F_{(1/59)} = 4.918$, $p = 0.030$), whereas the difference for TMT-A remained insignificant ($F_{(1/59)} = 0.098$, $p = 0.755$). Effects of diurnal preference with a better performance of morning oriented participants emerged in both TMT-A ($F_{(1/59)} = 4.144$, $p = 0.046$) and TMT-B ($F_{(1/59)} = 8.244$, $p = 0.006$). Significant main effects of "time" indicating an overnight improvement of performance were observed for both TMT-A ($F_{(1/59)} = 5.085$, $p = 0.028$) and TMT-B ($F_{(1/59)} = 32.672$, $p < 0.001$). All interactions remained non-significant. With respect to the first test session, only one participant had a z-score of less than -1 in the TMT-A. In contrast, an increased proportion of subjects with deficient z-scores ($n = 12$, 19%) was found for TMT-B, but without a significant difference between MDD ($n = 9$) and HC ($n = 3$) ($\chi^2 = 2.639$, $p = 0.104$). Among these 12 subjects, the proportion of participants with evening preference (9 of 31) was higher than that with morning preference (3 of 33) resulting in a significant group difference ($\chi^2 = 3.964$, $p = 0.047$).

As shown in Fig. 3, HC had higher positive mood scores on the BSKE than MDD patients (main effect group: $F_{(1/59)} = 32.627$, $p < 0.001$). We did not observe main effects of diurnal preference ($F_{(1/59)} = 0.735$, $p = 0.395$) and time ($F_{(1/59)} = 0.560$, $p = 0.475$), nor further interactions (i.e. first- and second-order interactions between group, diurnal preference and time).

3.3. Attentional-executive functioning in patients with MDD: subgroup analysis of diurnal preference and sleep quality

In order to investigate the association of diurnal preference and sleep quality with cognitive performance in MDD patients, we carried out a subgroup analysis by further dividing the sample according to their severity of sleep quality impairment (PSQI ≤ 10 vs. > 10). The four groups were labeled as follows: "evening preference with no to moderately impaired sleep quality" ($n = 9$), "evening preference with severely impaired sleep quality" ($n = 9$), "morning preference with no to moderately impaired sleep quality" ($n = 7$), and "morning preference with severely impaired sleep quality" ($n = 9$). When comparing patients with evening preference to those with morning preference, significant group differences were neither found for the PSQI total score (10.3 ± 4.0 vs. 9.9 ± 4.6, $t = 0.272$, $p = 0.787$) nor regarding the frequency of cases with severely impaired sleep quality ($\chi^2 = 0.133$, $p = 0.716$). Group comparisons (evening vs. morning preference and no to moderately vs. severely impaired sleep quality, respectively) did not reveal any significant differences with respect to sex, age, education level, depression severity, diagnoses and psychopharmacological treatment (all $p$values > 0.1).

Neuropsychological data of the four aforementioned groups are displayed in Fig. 4. Again, poorer cognitive performance of patients with evening preference compared to patients with morning preference was shown by a significant main effect for TMT-A ($F_{(1/30)} = 7.255$, $p = 0.011$) and TMT-B ($F_{(1/30)} = 7.071$, $p = 0.012$). Patients with severely impaired sleep quality performed poorer than patients with no to moderately impaired sleep quality, irrespective of diurnal preferences as reflected by a significant main effect in the TMT-A ($F_{(1/30)} = 7.260$, $p = 0.011$) and TMT-B ($F_{(1/30)} = 6.674$, $p = 0.015$). Both results remained significant when Bonferroni-adjustment was applied ($\alpha = 0.025$ per tests). For MDD patients, a significant overnight improvement of performance was demonstrated for the TMT-B ($F_{(1/}$

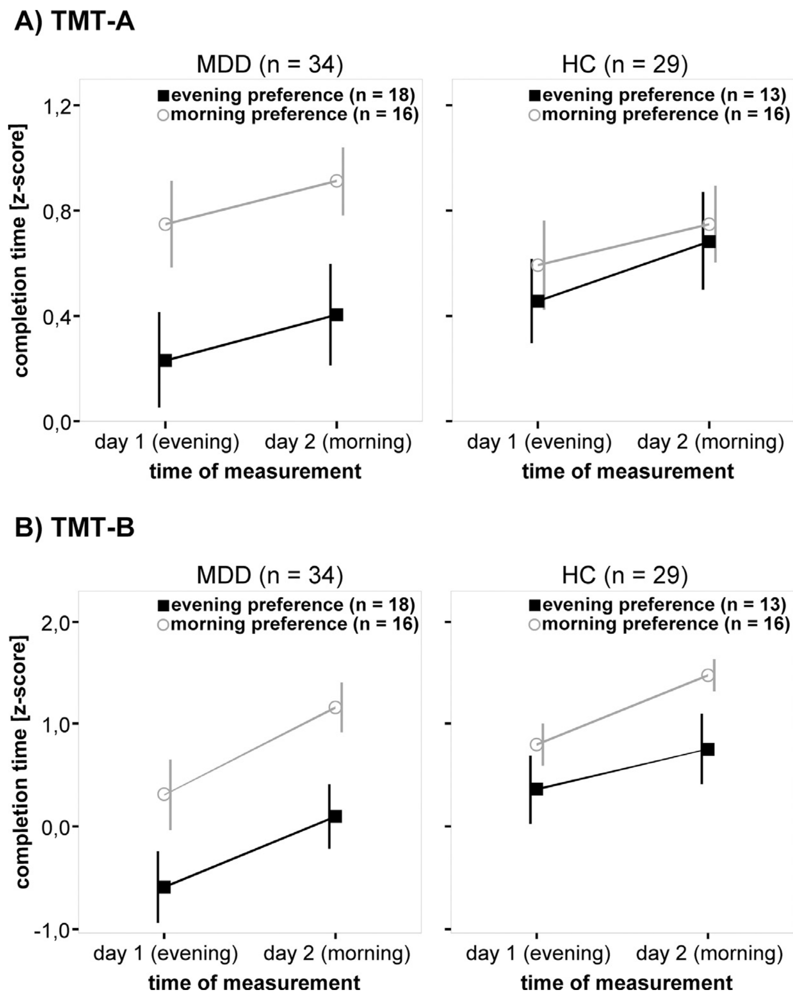

Fig. 2. Cognitive performance in patients with major depressive disorder (MDD) and healthy controls (HC) subdivided by diurnal preference ($M \pm$ SEM).

$_{30)}$ = 22.184, $p < 0.001$) but not for TMT-A ($F_{(1/30)} = 2.155$, $p = 0.152$). All interaction effects remained non-significant.

3.4. *Attentional-executive functioning in patients with MDD: correlations and ANCOVA subgroup analyses*

The BDI-II scores did neither correlate with TMT-A, nor with TMT-B at the evening as well as at the morning assessment ($p > 0.1$). A significantly positive association between the BSKE score and TMT-A emerged for the morning assessment ($r = 0.415$, $p = 0.015$), but not for the evening assessment. Similarly, all other correlations were weak ($r < 0.0.2$, $p > 0.2$). An ANCOVA including the BSKE as a covariate was applied and revealed that both, the effect of diurnal preference ($F_{1/28} = 9.329$, $p = 0.005$) and sleep quality ($F_{1/28} = 5.885$, $p = 0.022$) on the TMT-A, remained significant.

4. Discussion

In this study, diurnal preference, sleep quality and neuropsychological performance were assessed in patients with MDD and HC. We

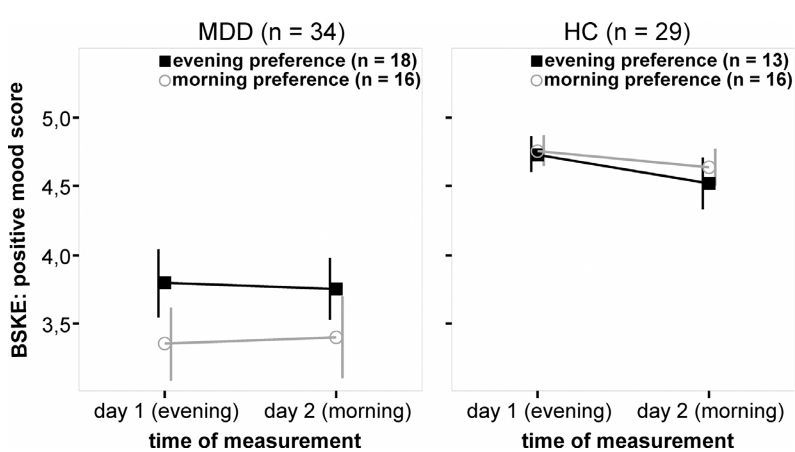

Fig. 3. Measures of current mood in patients with major depressive disorder (MDD) and healthy controls (HC) subdivided by diurnal preference ($M \pm$ SEM).

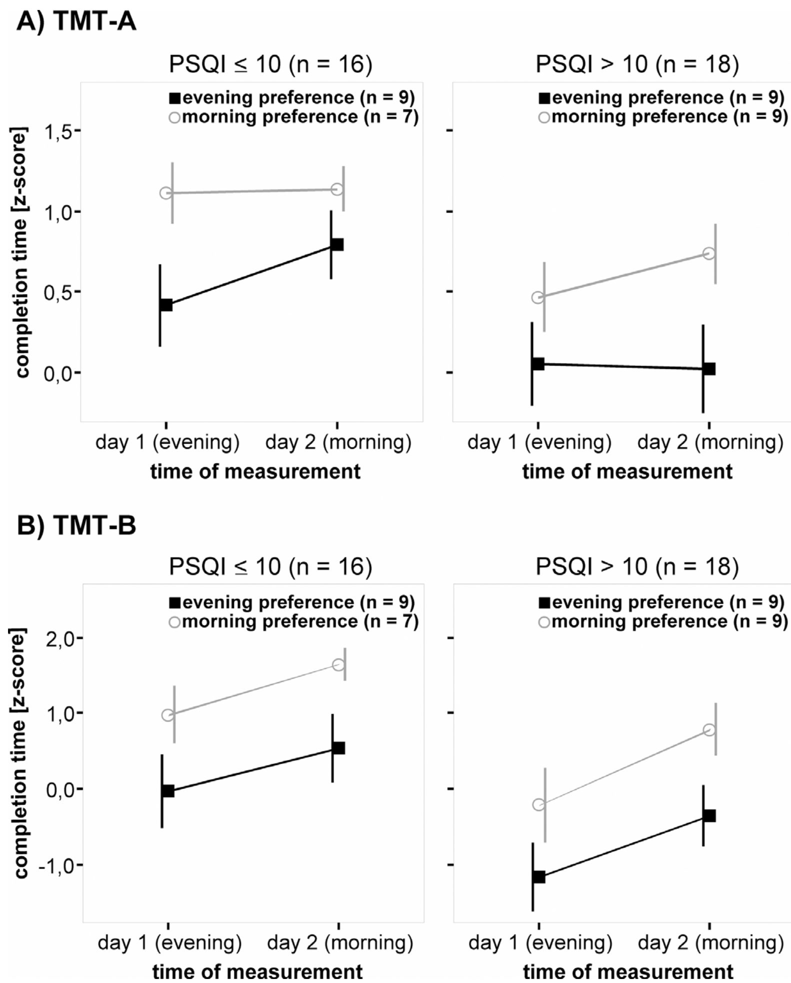

Fig. 4. Cognitive performance in patients with major depressive disorder (MDD) subdivided by diurnal preference and severity of poor sleep quality ($M \pm$ SEM).

found that evening oriented MDD patients and HC performed poorer on neuropsychological tasks than those with morning preference. Within the MDD group, cognitive performance was negatively affected by severity of poor sleep quality, independent of diurnal preference.

Supporting our hypothesis, MDD patients performed significantly poorer than HC on the TMT-B, but not on the TMT-A. Likewise, the proportion of participants performing one standard deviation ore more below the mean of a normative sample was higher for the TMT-B compared to the TMT-A, especially in MDD patients. This finding is consistent with a meta-analysis reporting better discriminative abilities between MDD and HC for tasks with additional demands on executive functions than for simple processing speed tasks (Snyder, 2013).

As a major result, evening oriented individuals (MDD and HC) performed significantly poorer on both, the TMT-A and TMT-B, than those with morning preference. Although an interaction between MDD vs. HC and diurnal preference did not reach statistical significance, the neuropsychological difference between the diurnal preference groups was descriptively more pronounced in MDD patients and statistically significant within the patient group in the subgroup analysis. This finding extends previous research on the relationship between diurnal preference and cognitive function in healthy individuals (e.g. Matchock and Mordkoff, 2009; Schmidt et al., 2015) by including a group of MDD patients who often exhibit executive deficits. The differences between evening and morning oriented MDD patients on the TMT could not be attributed to socio-demographic or the assessed clinical variables, since both groups were comparable in this regard. However, it cannot be ruled out that other clinical characteristics, which have been shown to be related with diurnal preference, might have contributed to this finding. Antypa et al. (2017) reported an association between evening preference and rumination, and rumination was found to be negatively related to performance in processing speed and executive tasks in MDD (Schwert et al., 2017). Poor sleep quality is a clinical feature of MDD that was found to be associated with diurnal preference (Chan et al., 2014) which may affect neuropsychological performance. However, this was not supported by our data, since both, diurnal preference and sleep quality, independently affected cognitive performance. Both diurnal preference groups did neither differ in the PSQI global score nor in the proportion of patients with severely impaired sleep quality (PSQI score > 10).

Evening-oriented patients showed, irrespective of sleep quality, poorer cognitive performance than those with morning preference, wheras severely impaired sleep quality negatively affected cognitive performance in both diurnal preference groups. Results remained significant when controlling for current mood which was solely correlated with processing speed in the morning.

In summary, the results are in line with our hypothesis and with previous studies demonstrating that poor sleep quality, whether assessed subjectively or objectively, contributes to cognitive impairment in young to middle-aged people (Kundermann et al., 2016), and older depressive patients (Naismith et al., 2009).

Based on these findings, we conclude that both, evening preference and poor sleep quality, frequently occuring before and persisting after a depressive episode (Lustberg and Reynolds, 2000), are contributing to cognitive impairment in MDD. With regard to the neurobiological mechanisms of how poor sleep affects cognition, several functional imaging studies have identified the prefrontal cortex as a brain region which plays a crucial role for attentional-executive control abilities and which is particular susceptible to altered functioning in the presence of sleep disturbance (e.g. Altena et al., 2008). Up to date, only a few studies investigated neurobiological mechanisms underlying the association between diurnal preference and cognitive performance. A very recent resting-state fMRI study reported poorer attentional performance related to lower functional connectivity in the brain's default mode network (DMN) in evening-oriented healthy controls compared to morning-oriented subjects. Functional connectivity of some DMN regions (e.g. in the medial prefrontal cortex) was also found to predict attentional performance (Facer-Childs et al., 2019). Adding to this, differences between the diurnal preference types in the white matter microstructure of various brain regions, including the frontal lobes, were shown with diffusion tensor imaging (Rosenberg et al., 2014). Evening oriented individuals exhibit a chronic “jet lag” due to the mismatch between their internal circadian timing and external constraints, which was found to be associated with cognitive deficits accompanied by higher cortisol levels and structural brain changes (Cho, 2001).

It should be noted that we did not find any effects of daytime and diurnal preference on current mood, particularly in MDD patients. This was probably due to sample characteristics since patients with melancholic features – known for their diurnal mood variations (Hyett et al., 2008) – were not present in the study sample. On the other hand, this aspect resulted in a relative homogeneity of our patient sample, which was also improved by the predefined inclusion criteria such as the age-range between 18 and 50 years (in order to exclude older subjects and thereby to minimize the possibility of neurodegerative or age-associated changes) and choosing 5 days as a period for stable medication, as most antidepressants and related drugs are in a pharmacokinetic steady state within this time period.

A main limitation of our study was the small sample size, which did not allow subgroup analysis applying the usual classification of (three) chronotypes. The neuropsychological assessment was not comprehensive and reflected only a subdomain of executive functions. Finally, our design was not appropriate to specifically address diurnal differences of cognitive functioning, and especially the synchrony effect, since the fixed sequence of assessments promoted practice effects. It may therefore be even more remarkable that morning oriented MDD patients performed better than those with evening preference even at their non-preferred time of day (i.e. during the first evening assessment).

In summary, the present study demonstrates, to our knowledge for the first time, that both, evening preference as a trait-like characteristic and severely impaired sleep quality, contribute additively to poorer cognitive performance in MDD, independent of current mood. Accordingly, poorer cognition was more likely in those patients, who exhibited evening preference accompanied with severely impaired sleep quality. The findings need to be replicated in studies with larger numbers of MDD patients. It would be valuable to investigate the neurobiological mechanisms underlying the observed associations between evening preference, poor sleep, and cognitive impairment in MDD. From the treatment perspective, chronobiological interventions as well as cognitive-behavioral techniques that specifically target poor sleep may be promising to improve cognition in MDD. Indirect evidence for such an effect comes from a recent study demonstrating that elderly patients with mild cognitive impairment and comorbid insomnia show improved cognition after cognitive-behavioral therapy for insomnia (Cassidy-Eagle et al., 2018). So far, similar studies in MDD patients are missing.

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