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Preliminary support for the role of reward relevant effort and chronotype in the depression/insomnia comorbidity

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Abstract

Background: The presence of insomnia in the context of depression is linked to a number of poor outcomes including reduced treatment response, increased likelihood of relapse, and greater functional impairment. Given the frequent co-occurrence of depression and insomnia, research into systems and processes relevant to both disorders, specially reward processing and circadian rhythm disruption, may help parse this complex comorbidity.

Methods: A pilot study was conducted on a sample of 10 veterans with clinically significant depression and insomnia symptoms. Participants completed objective (actigraphy) and subjective (sleep diary) assessments of sleep, self-reports of chronotype, and behavioral tasks assessing reward relevant effort before and after 6 sessions of Cognitive Behavioral Therapy for Insomnia.

Results: Insomnia and depression significantly improved following CBT-I. Subjective sleep parameters significantly improved with large effect sizes. Actigraphy results were nonsignificant, but effect sizes for sleep efficiency and onset latency were in the medium range. Chronotype shifted significantly toward morningness following CBT-I, and an earlier chronotype at baseline was associated with increased reward effort following treatment. Changes in chronotype, depression and insomnia were not associated with changes in effort.

Limitations: Findings are limited by small sample size and lack of randomized control group.

Conclusions: Findings should be interpreted as hypothesis generating in the service of furthering research aimed at uncovering potential mechanisms underlying the depression/insomnia comorbidity. Analyses of sleep data in extant datasets of reward processing impairments in depression as well as original projects aimed at exploring potential sleep, circadian rhythm, and reward interactions in depression are encouraged.

Introduction

Sleep disturbances, such as difficulty falling and staying asleep and early morning awakenings, are among the diagnostic criteria for major depressive disorder (MDD); however, approximately two-thirds of individuals with depression experience sleep disturbance that meets criteria for insomnia disorder (Franzen & Buysse, 2008). Insomnia comorbid with depression increases the likelihood of depression relapse, treatment non-response, and functional impairment (Franzen & Buysse, 2008). There is evidence, albeit somewhat mixed, that independent treatment of insomnia improves depression (Taylor et al., 2014), suggesting that insomnia and depression may share common biological underpinnings or may affect one another via a mediating pathway.

Two promising mechanistic targets are the circadian and reward systems, as dysfunctions in both have been implicated as core features of depression and may be meaningfully linked to insomnia. A core strategy of cognitive behavioral therapy for insomnia (CBT-I) is regularization of sleep/wake routines which may stabilize internal rhythms (Asarnow et al., 2013). Circadian rhythms are known to be disrupted in depression (Ehlers et al., 1993) and an evening chronotype, or a propensity for later peak alertness and sleep onset, has been independently associated with depression severity and non-remission (Chan et al., 2014) and poor sleep quality (Gianotti et al., 2002). Shifts toward morningness have been observed following sleep treatment and associated with improvements in depression and positive affect (Hasler et al., 2016), but have yet to be tested with behavioral measures of reward functioning. Reward processing is broadly impaired in depression, and modulation of the reward system may play a role in depression treatment (Dichter et al., 2009). Finally, there is a dearth of research on the effects of insomnia symptoms on reward function; however there is some evidence that disturbed sleep is associated with reward processing (Casement et al., 2016; Engle-Friedman et al., 2003).

As a preliminary step in examining these complex relationships, we conducted a pilot study that assessed sleep disturbance, chronotype, depression, and reward effort before and after treatment with CBT-I in veterans with clinically significant insomnia and depressive symptoms. In line with the literature, we hypothesized that insomnia symptoms, depression symptoms, and effort would improve following treatment, and chronotype would shift toward morningness. As chronotype has been proposed to have both state and trait like qualities (Hasler et al., 2016), we also examined how baseline as well as changes in chronotype influenced depression, insomnia, and effort changes.

Methods

Participants:

Participants were 17 veterans (12 male) with depressive symptoms defined as a Patient Health Questionnaire (PHQ-9; Martin et al., 2006) score >10 per VA/DoD Guidelines (2016) and clinically significant insomnia (defined as Insomnia Severity Index (ISI; Morin et al., 2011), scores >10) respectively. Seven participants dropped out or were withdrawn for the following reasons: need for higher level care (n=1); lack of childcare (n=1); development of a prolonged medical illness (n=1); substance use disorder following consent (n=1); job

change (n=1) and loss to follow-up (n=2). The final sample included 10 veterans ages 28 – 66 (8 male; M_{age} 47.5 [SD_{age} 12.9] years).

Participants were excluded for presence of psychotic symptoms, substance abuse, active suicidal/homicidal ideation, homelessness or sleep apnea. Veterans with PHQ-9 scores that met VA/DoD guidelines for treatment received depression treatment throughout the study protocol in the form of psychotherapy, clinical care management, and/or pharmacotherapy. No significant depression treatment changes were made during the study protocol.

Procedure:

All procedures were approved by the IRB of the Cpl. Michael J. Crescenz VA Medical Center. Following screening, veterans completed the Morningness Eveningness Questionnaire (MEQ; Horne & Östberg, 1976) and were fitted with an actigraph and instructed to complete a sleep diary for 7 nights while wearing the device. After actigraphy veterans completed the Effort Expenditure for Rewards Task (EEfRT; Treadway et al., 2009), immediately followed by session 1 of CBT-I. CBT-I was conducted in 6 sessions delivered by the PI in a manualized format for consistency. Sessions focused on psychoeducation about sleep, stimulus control strategies (e.g., getting out of bed when not sleepy, maintaining a regular sleep/wake routine, avoiding daytime napping) and sleep restriction guidelines (e.g., reducing time in bed to the total number of hours of sleep reported each night, not less than 5 hours). Sessions also focused on reducing cognitive and somatic hyperarousal and relapse prevention. The final session of CBT-I was followed by a repeat actigraphy/sleep diary session, and re-assessment of reward effort (EEfRT) and chronotype (MEQ).

Materials:

Insomnia Severity Index—The ISI is a 7-item questionnaire used to assess the severity of insomnia symptoms utilizing a 5-point Likert scale. Internal consistency is excellent with good convergent validity. An ISI score of 10 has been shown to be a reliable cutoff for clinically significant insomnia in community samples (Morin et al., 2011).

Patient Health Questionnaire—The PHQ-9 is a 9-item self-report instrument used widely in the VA to assess depression severity. PHQ-9 scores of < 10, 10–14, 15–19, and >20 represent absent, mild, moderate, and severe depression, respectively.

Sleep Diary—Participants record their subjective estimates of sleep time, wake time, number of awakenings, length of awakenings, naps, and subjective sleep quality every night. Diaries served as best practice procedures for scoring actigraphy and as guidelines for establishing sleep/wake routines in CBT-I.

Actigraphy—Subjects wore an Actiwatch-2 (Phillips) at two time points for one week each. The methodology is commonly used to record sleep/wake patterns over several days and has reasonable agreement with polysomnography in validation studies (Ancoli-Israel et al., 2003). Actigraphy provided standard sleep parameters including total sleep time, sleep efficiency, wake after sleep onset, and onset latency. Data were recorded in 1-minute epochs

with a wake threshold of 40 activity points and scored with Respironics Actiware software guided by self-reported sleep diaries to determine sleep intervals.

Morningness Eveningness Questionnaire.—The MEQ is a self-report measure of chronotype, or circadian preference. Individuals are asked to report on the timing of peak alertness and performance for a number of different activities. The measure assesses “Morningness” (i.e., the tendency to feel most alert in the early morning) vs. “Eveningness” (i.e., feeling most alert in the late evening). Morningness has been found to correlate with circadian pacemaker timing (Duffy et al., 2001).

Effort Expenditure for Rewards Task (EEfRT)—The EEfRT is a computerized multi-trial task in which participants choose between “hard” or “easy” tasks in order to obtain monetary rewards. Participants must make repeated manual button presses within a short period of time in order to raise the level of a virtual “bar” that appears on screen and can win rewards if they raise the bar in the allotted time. Participants choose between an “easy” task with a low reward (e.g., \$1.00), and a “hard” task with a higher reward up to \$4.00. Not all trials are “win” trials, meaning that some did not provide monetary payouts despite successful completion. The proportion of hard choices was selected as an index of willingness to put forth effort to receive monetary rewards. The EEfRT has demonstrated good test re-test reliability (Reddy et al., 2015).

Data analysis—Analyses were completed using SPSS Version 20. Changes in sleep parameters, chronotype and reward motivation were estimated with paired t-tests. Due to small samples size, non-parametric Wilcoxon Rank tests were conducted in tandem. As there were no changes in the pattern of results, parametric results and effect sizes are reported. Reward motivation was calculated as the proportion of hard choices made out of the first 50 as per Treadway et al., (2009). Data from one participant was dropped due to invariant responding (choosing the easy choice 100% of the time at both time points) and thus was considered invalid. The associations of chronotype and reward effort, depression, and insomnia were assessed via linear regression. Post-hoc associations of changes in effort, chronotype, insomnia and depression were assessed with Pearson correlations.

Results

Means and standard deviations of study variables are presented in Table 1. Insomnia significantly improved following CBT-I as measured by self-reported ISI ($t(9) = 3.57, p = .006$), and daily diary averages of sleep duration ($t(9) = -3.54, p = .006$), sleep efficiency ($t(9) = -6.22, p < .001$), wake after sleep onset ($t(9) = 3.98, p = .01$), and onset latency ($t(9) = 5.59, p < .001$). Sleep parameters were not significantly different when measured by actigraphy, although effect sizes for sleep efficiency and sleep onset latency were in the medium range (see Table 1). Depression was significantly reduced following treatment ($t(9) = 5.54, p < .001$). There was a significant shift in chronotype toward morningness following treatment ($t(9) = -3.66, p = .005$). Post-hoc analyses of wake time did not show a significant shift toward earlier awakenings, however. Proportion of hard choices on the EEfRT task did not change following treatment ($t(8) = .781, p = .46$).

An earlier chronotype at baseline (higher scores on the MEQ) was associated with increased selection of hard choice following CBT-I ($B = .015$; $p = .003$). Baseline MEQ was not significantly associated with depression or insomnia improvement. Post-hoc analyses examined whether the improvements in depression and insomnia and shift toward morningness were associated with improvements in effort, but these associations were non-significant. Full results and effect sizes are presented in Table 2.

Limitations

The results from the pilot study presented here should be interpreted as hypothesis generating rather than hypothesis confirming. While our analyses were grounded in theory, the small sample size, lack of control group, and self-report nature of symptoms increase the likelihood of sampling error. Moreover, our study examined depressive symptoms in the mild to moderate range as opposed to MDD diagnoses, and lacked objective assessments of circadian rhythms. Thus, the present findings cannot be considered evidence of disorder mechanisms, but may serve to generate more finely tuned hypotheses about how sleep, circadian rhythms, and reward processes may interact in depression.

Conclusions

Although these preliminary findings should be interpreted cautiously, they are in line with previous reports of improvements in both insomnia and depression symptoms following treatment with CBT-I. The lack of significant objective changes in sleep parameters is consistent with research that has repeatedly demonstrated discrepancies in objective vs. subjective reporting of sleep (Vanable et al., 2000). The shift toward morningness following CBT-I adds to previous reports of chronotype shifts following treatment (Corruble, et al., 2014; Hasler et al., 2016); however wake time was not significantly earlier post treatment. It is possible the shift toward morningness is reflective of better morning alertness and/or affect from improved sleep rather than a true shift in circadian rhythms. This should be more closely examined in future research.

To our knowledge, this study is the first to examine behavioral measures of reward functioning in the context of insomnia and circadian preference in depressed individuals. Given research associating evening chronotype with worse depression presentation (Hidalgo et al., 2009), and morningness with less severe presentation (Selvi et al., 2010), however, our finding that baseline morningness was associated with greater reward improvement could reflect greater depression improvement among those with less severe depression at baseline. Our data show a large but nonsignificant correlation between baseline PHQ-9 and baseline MEQ ($r = -0.73$, $p = .78$). As small amounts of variability can affect significance in small samples, future studies in larger samples should examine whether morningness may be independently related to reward effort.

Despite aforementioned limitations, findings from this study can be used as potential springboards for broader examinations of the complex relationship of insomnia and depression and the numerous neural circuits and biological systems involved. Researchers focused on reward dysfunction in depression are encouraged to re-examine extant datasets to

explore the role that sleep disturbance and circadian rhythms may play in reward functioning. Though not the most precise test of sleep disturbance, sleep items from depression rating scales and diagnostic interviews may prove to be useful variables in disentangling differential reward processing in depressed and healthy individuals. Likewise, the addition of sleep inventories and measures of chronotype into ongoing research projects can help characterize how sleep disturbance may impact reward function. Ideally, new research pursuits into this domain would also incorporate objective assessments of sleep and circadian functioning.

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Highlights

- Treatment with Cognitive Behavioral Therapy for Insomnia (CBT-I) yielded significant reductions in insomnia and depression symptoms in Veterans.
- There was a significant chronotype shift toward morningness following treatment with CBT-I
- Early chronotype at baseline was associated with increases in reward-relevant effort following treatment.
- Findings suggest sleep, circadian rhythms, and reward processing may be useful targets for generating testable hypotheses of the mechanisms underlying the insomnia/depression comorbidity.

Table 1.

Means and standard deviations of study variables pre and post treatment with CBT-I.

	Baseline	Post CBT-I	Change	Cohen's d
ISI	20.6 (2.41)	11.4 (7.9)	$p = .006$	1.13
PHQ-9	16.1 (3.78)	6.5 (4.5)	$p < .001$	1.75
MEQ	46.2 (10.27)	54 (8.7)	$p = .005$	1.15
EEfRT task % hard choices	35% (21%)	30% (17%)	NS	0.26
Actigraphy *				
Duration	339.71 (75.33)	358.08 (77.79)	NS	-0.17
Onset Latency	62.02 (36.44)	35.2 (26.6)	NS	0.58
Wake after Sleep Onset	60 (33.76)	46.6 (33.45)	NS	0.31
Sleep Efficiency	68% (8%)	78% (16%)	NS	-0.68
Sleep Diary *				
Duration	275.4 (110.4)	368.4 (74.4)	$p = .006$	-1.12
Onset Latency	88 (40.5)	17.66 (16.9)	$p < .001$	1.76
Wake after Sleep Onset	45.5 (46.16)	17.23 (22.91)	$p = .01$	0.98
Sleep Efficiency	60% (17%)	86% (13%)	$p < .001$	1.97

* Sleep data are presented in minutes

Table 2.

Regression Analyses of Baseline MEQ predicting changes in effort, insomnia and depression.

	B	SE	Beta	t	p	R² Change
Model 1. EEfRT Change	0.015	0.004	0.817	3.747	0.007	0.667
Model 2. Insomnia Change	0.215	0.269	0.272	0.799	0.447	0.074
Model 3. Depression Change	-.039	0.188	-0.073	-0.206	.842	.005

Table 3.

Associations among changes in insomnia, depression, chronotype, and effort following treatment with CBT-I.

	ISI Change	PHQ-9 Change	MEQ Change
PHQ-9 Change	.799 **		
MEQ Change	−0.486	−0.221	
EEfRT Change	0.112	0.291	−0.643

**
=significant at .01