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Shifts towards morningness during behavioral sleep interventions are associated with improvements in depression, positive affect, and sleep quality

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Abstract

Morningness-eveningness (M-E) is typically considered to be a trait-like construct. However, M-E could plausibly shift in concert with changes in circadian and/or homeostatic processes. We examined M-E changes across three studies employing behavioral or pharmacological sleep treatments. Baseline/post-treatment M-E scores were strongly correlated across all three samples. M-E showed small, but systematic changes towards morningness in sleep-disturbed military veterans receiving behavioral interventions. No systematic M-E changes were observed in the two pharmacological studies (sleep-disturbed military veterans and adults with primary insomnia, respectively). In the behavioral study, M-E changes correlated with changes in depression, positive affect, and sleep quality. M-E changes also correlated with changes in positive affect in the adult insomnia group. M-E appears to exhibit state-like aspects in addition to trait-like aspects.

Keywords

morningness-eveningness; insomnia; sleep; mood; treatment

INTRODUCTION

Morningness-eveningness (M-E), also known as chronotype or circadian preference, is typically considered to be a trait-like construct (e.g., Klei et al., 2005), showing developmental shifts over the lifespan (Adan et al., 2012; Roenneberg, Wirz-Justice, & Mellow, 2003) but relatively stable over short time periods (Greenwood, 1994; Guthrie, Ash, & Bendapudi, 1995). However, M-E appears to be influenced by both circadian phase and homeostatic sleep drive (Emens et al., 2009; Mongrain, Carrier, & Dumont, 2006), and thus it may change more rapidly with acute alterations in these processes. Furthermore, only limited data supports the stability of M-E over short time frames of weeks to months (Greenwood, 1994; Guthrie, et al., 1995), and until recently, no studies examined the stability of M-E during treatment. Natale and colleagues (2008) reported that 46 female patients with eating disorders showed both increases in morningness and decreases in eating disorder symptoms after two months of cognitive behavioral therapy. A 2013 open trial of agomelatine in 721 patients with major depression also showed shifts towards morningness

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at both the 2- and 8-week assessments (Corruble et al., 2014), consistent with agomelatine acting in part via circadian mechanisms (e.g., Kasper et al., 2010). Notably, no studies have examined M-E changes following behavioral sleep treatments, although such treatments are aimed at manipulating circadian and homeostatic processes.

Prior studies suggest that M-E is influenced by circadian and homeostatic processes (Emens, et al., 2009; Mongrain, et al., 2006). Based on the Two Process Model of Sleep, periods of sleep and wakefulness are largely a product of two interacting processes: a circadian rhythm in alertness, and a homeostatic sleep drive that accumulates with time spent awake (Borbely, 1982). Consistent with this model, evidence suggests that greater eveningness may be related to later circadian timing, more slowly accumulating and dissipating homeostatic sleep drive, or both. Notably, behavioral sleep treatments target these same processes, such as using sleep restriction to increase homeostatic sleep drive, and regularizing wake time to stabilize circadian phase (Germain et al., 2014). Behavioral sleep treatments may thereby impact M-E. However, although interventions such as appropriately-timed bright light and melatonin, as well as systematic changes to sleep/wake schedules, all have demonstrable effects on circadian timing (Minors Waterhouse 1991; Cajochen Krauchi 2003; Burgess & Eastman 2006), the effects of behavioral sleep treatments for insomnia on the circadian correlates of M-E remain unknown.

Changes in M-E could plausibly be related to other clinical outcomes. A large body of evidence links eveningness to increased depression, lower positive affect, and greater sleep disturbance (e.g., Drennan, Klauber, Kripke, & Goyette, 1991; Hasler, Allen, Sbarra, Bootzin, & Bernert, 2010; Hasler et al., 2012; Kitamura et al., 2010), along with other behavioral and personality constructs (reviewed in Adan, et al., 2012). Accordingly, morningness predicted the antidepressant response to treatment in the aforementioned agomelatine trial, and those authors suggested that a malleable M-E thus has the potential to be a treatment target (Corruble, et al., 2014). As such, treatments that effectively influence M-E may, in turn, improve both affective functioning and sleep.

In the present paper, we conducted secondary analyses of three independent sleep treatment studies to address two aims. For our primary aim, we investigated whether M-E changed in response to behavioral and/or pharmacological sleep interventions in military veterans reporting sleep disturbance (Studies 1 and 2) or adults diagnosed with primary insomnia (Study 3). Given that behavioral sleep treatments target circadian and homeostatic processes, we predicted the military veterans receiving brief behavioral treatment for insomnia (Study 1) would show significant shifts towards morningness. We were agnostic about the direction of systematic M-E changes in the two pharmacological studies: comparing prazosin versus placebo in Study 2 and comparing escitalopram, zolpidem, and placebo in Study 3. However, given the bidirectional associations between sleep and circadian function, it seemed plausible that these sleep treatments could also influence M-E.

For our secondary aim, we examined whether any observed changes in M-E were accompanied by concomitant changes in overall depression, positive or negative affect, sleep quality, or diary-based sleep timing. We predicted that shifts towards morningness would be correlated with decreases in depression and increases in positive affect and sleep quality. We

also predicted that shifts towards morningness would correlate with advances in diary-based sleep timing. We did not predict any correlated changes in negative affect given previous data suggesting that M-E is unrelated to negative affect (Hasler, et al., 2010; Hasler, et al., 2012).

METHODS

Participants and treatments

Participants were drawn from three independent studies testing behavioral or pharmacological treatments for sleep disturbance. The studies were approved by the University of Pittsburgh Institutional Review Board and all participants provided written, informed consent. Demographics are reported in Table 1. Only participants with baseline and post-treatment M-E assessments were included.

Studies 1 and 2 were composed of military returnees from Operation Iraqi Freedom and Operation Enduring Freedom reporting chronic insomnia (lasting >1 month). Exclusion criteria were the presence of diagnosed or suspected sleep breathing disorder, another sleep disorder requiring treatments other than behavioral insomnia treatments (e.g., restless leg syndrome), untreated, current, and severe major depression, any psychotic disorders, untreated and/or unstable psychiatric or medical disorders, bipolar disorder, and active substance abuse and/or dependence in the past 3 months. The Structured Clinical Interview for DSM-IV (First, Gibbon, & Spitzer, 1997) was used to assess past and current psychiatric symptoms. An overnight polysomnographic (PSG) sleep study evaluated sleep-disordered breathing, in conjunction with the Structured Clinical Interview for DSM-IV Sleep Disorders (developed locally) to evaluate symptoms of DSM-IV sleep disorders in general. Study 1 also excluded for untreated, current, and severe posttraumatic stress disorder (PTSD), whereas Study 2 specifically recruited military veterans meeting diagnostic criteria for current PTSD. The Clinician Administered PTSD Scale (Blake et al., 1995) was used to evaluate past and current PTSD symptom severity in Studies 1 and 2.

In Study 1, 40 military veterans were randomly assigned to one of two behavioral treatment conditions over four weeks; 29 completed treatment and had pre- and post-treatment M-E scores. Fourteen participants were assigned to brief behavioral treatment for insomnia, adapted for military veterans (BBTI-MV), while 15 participants were assigned to information control. Both conditions included two in-person visits (weeks 1 and 3) and two telephone contacts (weeks 2 and 4) with a masters' level therapist. The BBTI-MV treatment, described in more detail elsewhere (Germain, et al., 2014), consists of education about healthy sleep practices, sleep restriction, and stimulus control. In the BBTI-MV condition, the participant was prescribed a specific sleep schedule and received tailored strategies for stimulus control and adherence promotion. In the information control condition, participants received brochures containing information about insomnia and healthy sleep practices, including a description of stimulus control, but did not receive tailored recommendations on how to apply the principles to their own sleep.

In Study 2, 36 military veterans were randomly assigned to one of two pharmacological treatment conditions over eight weeks; 25 completed treatment and had pre- and post-

treatment M-E scores. Eleven participants were assigned to the active condition (prazosin), while 14 participants were assigned to the placebo condition. In the original study, prazosin (an alpha-1 antagonist) was hypothesized to effectively treat nightmares and insomnia by attenuating central noradrenergic tone during sleep. Both prazosin and placebo were administered as an oral dose of four capsules 30 minutes prior to bedtime. Prazosin was titrated up from an initial dose of 1 mg, increasing over the subsequent weeks to a maximum of 15 mg. The decision alter or stop the scheduled dose increase was made weekly by a treatment-blinded physician and research pharmacist based on response, risks, and side effects. At the end of treatment, the final mean nightly dose of prazosin was 11.5 mg (SD=4.4 mg; 4–15 mg).

In Study 3, 58 adults meeting DSM-IV criteria for primary insomnia, and with pre- and post M-E scores, were randomly assigned to one of three pharmacological treatment conditions over eight week: escitalopram (n=20), zolpidem (n=19), or placebo (n=19). Three participants in the escitalopram group received citalopram instead. In the original study, these agents were administered as probes of affect dysregulation (escitalopram) and sleep/wake disturbance (zolpidem) as important correlates and potential mechanisms of insomnia. Exclusion criteria included significant or unstable medical conditions, current major syndromal psychiatric disorders, other current sleep disorders beyond primary insomnia, medications known to affect sleep or wake function, consumption of >4 cups of coffee per day, or more than 14 drinks of alcohol per week. As in Studies 1 and 2, the SCID-IV, sleep SCID, and an overnight PSG study were used to confirm study eligibility. Medications or placebo were administered as an oral dose of four capsules 30 minutes prior to bedtime. Both escitalopram and zolpidem were titrated up from an initial dose of 5 mg, increasing to maximum doses of 20 and 10 mg, respectively. Decisions to alter or stop the scheduled dose increases were made weekly by a treatment-blinded physician and research pharmacist based on response, risks, and side effects. At the end of treatment, the final mean nightly doses of 17.9 mg (SD=3.6 mg; 5–20 mg) for escitalopram and 10.0 mg (SD=0.0 mg; 5–10 mg) for zolpidem. (The three participants receiving citalopram all had final doses of 40 mg.)

Studies were conducted in Pittsburgh, Pennsylvania, USA, throughout the calendar year, with no significant group differences in modal month of data collection (data available upon request).

Measures

All participants completed measures assessing M-E, depression, positive and negative affect, and sleep quality at baseline and post-treatment. Across all three studies, participants completed Composite Scale of Morningness (CSM; Smith, Reilly, & Midkiff, 1989) as a measure of M-E. We used the CSM as a continuous scale for our primary analyses, given the increased statistical power and the inconsistency in criteria for categorical assignment across the literature. We also classified participants by type using the scoring thresholds suggested by Natale and Alzani (2001): 13–26=evening-type; 27–41=intermediate-type, 42–55: morning-type. In Studies 1 and 2, participants completed the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996) as a measure of depressive symptomatology, while in Study 3 participants completed the Inventory of Depressive Symptomatology (IDS; Rush et

al., 1986). In all three studies, participants completed the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) as a measure of positive and negative affect. In Studies 1 and 2, the Past Week version of the PANAS was administered. In Study 3, participants completed a Right Now version of the PANAS approximately four times per day for up to 15 days at each time point, resulting in a mean of 27.5 (SD=5.7) assessments at baseline, and a mean of 22.3 (SD=7.0) assessments at post-treatment. We averaged across each time point's assessments to calculate PANAS scores for Study 3. Finally, participants in all three studies completed the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) as a measure of overall subjective sleep quality.

Sleep diary data at baseline and post-treatment were available for a subsample of Study 1 (n=22) and Study 2 (n=19) and all participants in Study 3. Participants completed the diary for a minimum of three days and for up to seven days at each time point in each study. Given the focus of behavioral sleep treatments on sleep timing, we focused on the *lights out* (the time participants attempted to fall asleep) and the *rise time* variables for the present analyses.

Data analysis

All analyses were conducted in SPSS version 21. We used mixed-effect models to examine changes in M-E over treatment. We ran separate models for each study, and included visit (baseline or post-treatment), treatment group, and the treatment group X visit interaction as predictors of interest. Age and sex were included as covariates. Type III tests are reported below, along with the 95% confidence intervals (CI) for the unstandardized estimates of the relevant model coefficients. We used Fisher's exact tests (FET) to compare the distribution of M-E types between baseline and post-treatment. We used Pearson's correlations to examine the relationship between baseline and post-treatment M-E in each study. We ran partial correlations to examine the relationship between change in M-E and change in depression, positive and negative affect, and sleep quality. Change scores were calculated by subtracting the baseline score from the post-treatment score. Age, sex, and treatment group were included as covariates.

RESULTS

Changes in morningness-eveningness (Table 1)

Study 1: Military veterans receiving BBTI or information control—Mean CSM scores increased (shifted towards morningness) from baseline to post-treatment across the entire sample ($F_{1,29}=13.35, p=0.001, 95\% \text{ CI}[-4.69, -0.38]$); change in CSM did not differ as result of receiving the active treatment or information control (Treatment X Visit: $F_{1,29}=0.10, p=0.76, 95\% \text{ CI}[-3.56, 2.63]$). Increasing age was associated with higher CSM scores overall ($F_{1,29}=5.41, p=0.03, 95\% \text{ CI}[0.03, 0.46]$). CSM scores did not differ by sex ($F_{1,29}=2.01, p=0.17, 95\% \text{ CI}[-13.77, 2.49]$). After accounting for age, CSM scores increased by an average of 2.53 points from baseline to post-treatment. Change in CSM scores ranged from +14 (towards greater morningness) to -2 (towards greater eveningness).

Across Study 1, four participants changed from evening-types to intermediate-types, and two participants changed from intermediate-types to morning-types. No participants shifted from intermediate- to evening-types, or from morning- to intermediate-types, and 23 did not change type. There was no significant change in the relative distribution of evening-, intermediate-, and morning-types from baseline to post-treatment ($FET=1.98$, $p=0.40$).

Study 2: Military veterans receiving prazosin or placebo—Mean CSM scores did not show a significant change from baseline to post-treatment across the entire sample ($F_{1,25}=1.32$, $p=0.26$, 95% CI[-2.74,1.03]), nor did change in CSM differ as a result of treatment (Treatment X Visit: $F_{1,25}=0.01$, $p=0.93$, 95% CI [-2.72,2.98]). Neither age ($F_{1,25}=0.17$, $p=0.68$, 95% CI[-0.42,0.63]) nor sex ($F_{1,25}=1.6$, $p=0.22$, 95% CI[-10.01,2.39]) was significantly associated with CSM score. Changes in CSM scores ranged from +7 to -9.

Across Study 2, two participants changed from evening-types to intermediate-types, and two participants changed from intermediate-types to morning-types. One participant changed from an intermediate- to an evening-type, two participants changed from morning- to intermediate-types, and 18 did not change type. There was no significant change in the relative distribution of evening-, intermediate-, and morning-types from baseline to post-treatment ($FET=0.49$, $p=1.00$).

Study 3: Adults with primary insomnia receiving escitalopram, zolpidem, or placebo—Mean CSM did not show any significant change from baseline to post-treatment across the entire sample ($F_{1,58}=0.14$, $p=0.72$, 95% CI[-0.54, 3.54]), nor did change in CSM differ as a result of treatment (Treatment X Visit: $F_{2,58}=2.10$, $p=0.13$, 95% CI[-5.52, 0.31]). Increasing age was associated with higher CSM scores ($F_{1,58}=14.80$, $p<0.001$, 95% CI[0.21,0.65]). CSM scores did not differ by sex ($F_{1,58}=0.10$, $p=0.76$, 95% CI[-4.78,3.49]). Changes in CSM scores ranged from +10 to -8.

Across Study 3, 2 participants changed from evening-types to intermediate-types, and 6 participants changed from intermediate-types to morning-types. Six participants changed from intermediate- to evening-types, two participants changed from morning- to intermediate-types, and 42 did not change type. There was no significant change in the relative distribution of evening-, intermediate-, and morning-types from baseline to post-treatment ($FET=2.21$, $p=0.34$).

Correlation between baseline and post-treatment morningness-eveningness

Baseline and post-treatment CSM scores were similarly and strongly correlated across all three studies (Study 1: $r=0.87$, $p<0.001$; Study 2: $r=0.84$, $p<0.001$; Study 3: $r=0.86$, $p<0.001$).

Correlation between changes in morningness-eveningness, positive affect, and sleep quality (Figure 1)

Given that treatment type was unrelated to change in M-E within each sample, we collapsed across treatments within each study to increase the statistical power to examine partial correlations between baseline-to-post-treatment changes in M-E (CSM), depression (BDI or

IDS), positive and negative affect (PANAS), and sleep quality (PSQI). All partial correlation analyses included age, sex, and treatment group as covariates.

Study 1: Military veterans receiving BBTI or information control—Shifts towards morningness were associated with decreases in depression ($\rho=-0.64$, $p=0.001$), increases in positive affect ($\rho=0.79$, $p<0.001$) and sleep quality ($\rho=-0.58$, $p=0.005$), but were unrelated to changes in negative affect ($\rho=0.08$, $p=0.71$).

Study 2: Military veterans receiving prazosin or placebo—Changes in M-E were unrelated to changes in depression ($\rho=-0.14$, $p=0.58$), positive affect ($\rho=-0.09$, $p=0.73$), negative affect ($\rho=0.19$, $p=0.43$), or sleep quality ($\rho=-0.27$, $p=0.26$).

Study 3: Adults with primary insomnia receiving escitalopram, zolpidem, or placebo—Shifts towards morningness were associated with positive affect ($\rho=0.35$, $p=0.02$), but were unrelated to changes in depression ($\rho=-0.10$, $p=0.47$), negative affect ($\rho=-0.09$, $p=0.54$) or sleep quality ($\rho=0.16$, $p=0.30$).

Changes in sleep timing and correlation with changes in morningness-eveningness (Table 1)

Study 1: There were no significant baseline-to-post-treatment changes in lights out ($t=-0.90$, $df=21$, $p=0.38$) or rise time ($t=0.59$, $df=21$, $p=0.57$). There were no significant associations between changes in M-E and respective changes in lights out ($r=0.36$, $p=0.10$) or rise time ($r=0.16$, $p=0.48$).

Study 2: There were no significant baseline-to-post-treatment changes in lights out ($t=1.08$, $df=18$, $p=0.30$) or rise time ($t=0.59$, $df=18$, $p=0.56$). Change in M-E correlated with both change in lights out ($r=0.49$, $p=0.03$) and change in rise time ($r=0.65$, $p=0.003$).

Study 3: There were no significant baseline-to-post-treatment changes in lights out ($t=-0.34$, $df=57$, $p=0.73$) or rise time ($t=-0.34$, $df=57$, $p=0.73$). Change in M-E was correlated with change in lights out at a trend level ($r=-0.26$, $p=0.05$) but was unrelated to change in rise time ($r=-0.18$, $p=0.17$).

DISCUSSION

We examined changes in M-E across three independent sleep treatment studies, and as predicted, we found that behavioral sleep interventions were associated with systematic shifts towards morningness. Although systematic changes in M-E were not apparent in either of the pharmacological treatment studies at the group level, we observed substantial inter-individual variability in M-E changes across treatment in both studies. Also as predicted, shifts towards morningness were associated with concomitant reductions in depression, increases in positive affect, and improvements in sleep quality. However, these effects were generally confined to the behavioral treatment study. Furthermore, although M-E showed substantial changes from baseline to post-treatment in a number of participants, baseline and post-treatment M-E scores were strongly correlated across all three studies, suggesting rank order stability. Taken together, our findings suggest that M-E is responsive

to behavior-focused sleep interventions and may reflect current sleep behavior as well as trait-like circadian preference. Given that shifts towards morningness were associated with improved affective and sleep functioning, M-E warrants further investigations aimed at clarifying and characterizing its potentially mechanistic role in behavioral sleep treatment. Such investigations should include measures that can disentangle how changes in the M-E measure relate to any changes in physiological and/or central indices of circadian phase and homeostatic drive.

To our knowledge, this is the first report of M-E showing a systematic response to behavioral sleep interventions. Notably, the shift towards morningness was consistent across both the “active” BBTI condition and the information control. That said, overlapping recommendations concerning stimulus control and health sleep practices were conveyed in both conditions, and thus it is plausible that the increased morningness preference reflects true circadian and/or homeostatic changes. (Indeed, as reported elsewhere (Germain, et al., 2014), the veterans in the information control condition also showed robust improvements in insomnia symptoms, suggesting this ostensible control served as a “therapist-enhanced bibliotherapy” in this particular population.) Based on this same reasoning, it is less surprising that the pharmacological treatments—none of which directly targeted circadian or homeostatic mechanisms—did not result in systematic M-E changes. Our results provide an interesting comparison to the agomelatine study by Corruble and colleagues (2014), who also observed systematic shifts towards morningness, potentially because of agomelatine’s action as a melatonin agonist (e.g., Kasper, et al., 2010). Notably, average M-E changes were of a similar magnitude (~3 points) in both studies. While this average extent of change is of questionable clinical significance, it remains striking that individual participants showed sufficient M-E changes to “switch categories”. Although the categorical shifts were not statistically significant among participants receiving behavioral sleep interventions, all the categorical shifts that did occur were in the direction of morningness. More direct targeting of M-E may result in larger systematic changes.

Both the systematic M-E changes in the behavioral treatment study and more unsystematic M-E changes observed among individuals in the two pharmacological treatment studies suggest that M-E has state-like qualities, and may partly reflect current sleep behavior. That said, the strong correlations between baseline and post-treatment M-E assessments support a trait-like aspect as well; that is M-E may shift in response to intervention, time, or other unknown factors, but these changes may be constrained to fluctuations around a “set-point”. This is consistent with other investigators’ conclusions that individuals maintain relative positions within the distribution of M-E while also undergoing systematic developmental changes in M-E: shifting towards eveningness during adolescence with a peak around age 20, then slowly progressing towards morningness for the rest of the lifespan (Roenneberg, et al., 2003). Given the support for trait-like aspects of M-E, one alternative hypothesis for the present results is that insomnia symptoms may have been “masking” the true circadian preference of some participants, and that successful behavioral treatment resulted in “unmasking” of relative tendencies towards morningness.

Although we predicted behavioral sleep treatments would induce a shift towards morningness, presumably via effects on homeostatic and circadian processes, one could

argue that sleep restriction instructions might induce a shift towards eveningness. That is, sleep restriction typically entails a delay in bedtimes while holding rise times relatively constant, which could presumably cause a phase delay due to relatively increased exposure to evening light. On the other hand, stimulus control instructions to maintain a regular rise time should reduce delayed rise times on weekends, presumably causing a phase advance due to relatively increased exposure to morning light. Interestingly, there were no significant changes in the available diary-based sleep times in any of the samples, contrasting with prior findings that behavioral sleep treatments influence sleep timing (Buysse et al., 2011; Germain et al., 2014). Furthermore, the only correlation between changes in sleep timing and change in morningness-eveningness occurred in one of the pharmacological studies (Study 2), suggesting that the systematic shift towards morningness in the behavioral treatment study is not simply a result of changes in sleep timing.

Our finding that shifting towards morningness was associated with improvements in depression, positive affect, and sleep quality complements a large body of cross-sectional research reporting parallel associations between morningness-eveningness and these other domains (e.g., Drennan, et al., 1991; Hasler, et al., 2010; Hasler, et al., 2012; Kitamura, et al., 2010). The lack of association with changes in negative affect is consistent with previous data and hypotheses that morningness-eveningness's relationship to depression is via appetitive motivation and reward pathways rather than the neural pathways associated with negative affect and behavioral inhibition (Hasler, et al., 2010; Hasler, et al., 2012). Recent neuroimaging findings support altered function in the reward circuit of evening-types ((Hasler, Sitnick, Shaw, & Forbes, 2013), including evening-types diagnosed with insomnia ((Hasler, et al., 2012), although these neural differences may extend beyond the reward circuit to other regions relevant to sleep, arousal, and affect regulation (Hasler, Insana, James, & Germain, 2013; Rosenberg, Maximov, Reske, Grinberg, & Shah, 2014)

An alternate interpretation of our findings is that the observed shifts towards morningness simply reflect participants feeling better in the morning as a result of treatment. Indeed, some CSM items emphasize functioning in the morning without explicit reference to timing, and several published factor analyses of the CSM and its variants have identified a "morning affect" factor in addition to factors more clearly linked to the timing of sleep and activity (Brown, 1993; Caci et al., 2005). Furthermore, the sleep restriction component has been previously shown to have time-of-day effects on alert cognition, particularly improving alertness at rise time (Miller, Kyle, Marshall, & Espie, 2013). However, this explanation—that M-E change is a non-specific effect or epiphenomenon of improvement in sleep and affective functioning—seems unlikely, given that participants generally improved across all three studies, but systematic changes in M-E were only observed in the behavioral study.

Limitations

Our analyses have several notable limitations. First, these were secondary analyses of existing datasets. Demonstrating that behavioral sleep interventions have a causal influence on M-E will require a study designed to test this question directly. We did not include any physiological measures of homeostatic sleep drive or circadian phase, and thus cannot speak to whether changes in these processes underlie the observed changes in self-reported M-E.

All three studies included relatively small samples, and thus our findings need to be replicated in larger samples. Our treatments were of differing lengths, and we did not include intermediate assessments of M-E in the pharmacological studies, and thus we cannot ascertain whether M-E showed initial systematic changes that diminished by later in treatment.

Conclusions

Overall, our findings suggest that M-E may have both state and trait-like characteristics. Consistent with evidence that M-E is influenced by circadian and homeostatic factors, M-E showed systematic changes in the context of behavioral sleep treatment targeting circadian and homeostatic processes. While we did not observe systematic M-E changes in the context of pharmacological sleep treatments, M-E showed substantial variability over time in some individuals, indicating that caution is required in utilizing a single assessment of M-E as a proxy for habitual circadian timing. Finally, given that M-E shifts are associated with changes in depression, affect, and sleep quality, M-E may deserve consideration as a treatment target unto itself.

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Figure 1. Scatterplots of the relationship between baseline-post-treatment change in morningness-eveningness (CSM score) and change in positive affect (PANAS-PA) across the three studies

Table 1

Demographics and clinical variables across baseline and post-treatment

	Study 1			Study 2			Study 3		
	Baseline	Post-treatment	Mean change	Baseline	Post-treatment	Mean change	Baseline	Post-treatment	Mean change
Sample	Military veterans in behavioral treatment			Military veterans in drug treatment			Adults with primary insomnia		
Treatment groups ^a	BBTI (n=14)	or information control (n=15)		Prazosin (n=11)	or placebo (n=14)		Escitalopram ^b (n=20), zolpidem (n=19), or placebo (n=19)		
Treatment length	4 weeks			8 weeks			8 weeks		
Age	39.01 (12.08)			27.63 (4.72)			35.73 (9.24)		
Males/females	25/4			20/5			26/32		
CSM	33.10 (7.73)	35.86 (8.28)	2.76 (4.12)	35.16 (6.39)	35.96 (5.99)	0.80 (3.50)	33.16 (8.67)	33.34 (9.24)	0.19 (4.76)
CSM type	7 E, 17 I, 5 M	3 E, 19 I, 7 M		2 E, 17 I, 6 M	1 E, 18 I, 6 M		14 E, 33 I, 11 M	18 E, 25 I, 15 M	
BDI	5.79 (5.32)	3.07 (3.91)	-2.72 (5.89)	6.12 (3.69)	4.84 (4.01)	-1.28 (4.80)			
IDS ^c							16.55 (6.28)	9.11 (6.98)	-7.44 (7.00)
PANAS									
Positive affect	30.57 (7.91)	33.68 (7.94)	3.11 (8.35)	28.96 (7.86)	32.32 (7.36)	3.36 (6.90)	22.45 (6.27)	22.51 (6.72)	0.06 (3.23)
Negative affect	14.00 (4.38)	13.67 (2.90)	-0.35 (3.24)	16.76 (5.21)	14.75 (4.66)	-1.88 (7.69)	12.51 (2.89)	12.35 (3.16)	-0.17 (1.93)
PSQI	10.61 (3.59)	6.64 (3.41)	-3.96 (4.00)	8.23 (3.16)	6.59 (3.86)	-1.63 (3.20)	11.42 (3.18)	8.78 (3.99)	-2.64 (4.15)
Sleep diary ^d									
Lights out	0:25 (1:37)	0:33 (1:28)	-0:07 (0:38)	0:04 (1:22)	23:48 (1:21)	0:15 (1:02)	23:56 (1:17)	23:58 (1:20)	-0:02 (0:44)
Rise time	7:45 (1:52)	7:37 (1:56)	0:07 (0:59)	7:48 (2:27)	7:33 (1:30)	0:15 (1:50)	7:13 (1:34)	7:15 (1:30)	-0:02 (0:53)

NOTE: Mean change was calculated as post-treatment score minus the baseline score.

^aData were collapsed across treatment groups within each study given that the CSM changes did not differ according to treatment group.^bThree participants received citalopram instead of escitalopram.^cThree participants in Study 3 had missing IDS-SR data (n=55).^dSeven participants in Study 1 and six participants in Study 2 had missing diary data.

CSM=Composite Scale of Morningness; CSM types: E=evening-type, I=intermediate-type, M=morning-type; BDI=Beck Depression Inventory; IDS=Inventory of Depressive Symptomatology; PANAS=Positive and Negative Affect Schedule; PSQI=Pittsburgh Sleep Quality Index