Sleep and Inhibitory Control Over Mood-Congruent Information in Emerging Adults With Depressive Disorder

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ABSTRACT

Objective: Accumulating evidence has suggested bidirectionality between sleep problems and depression, but the underlying mechanism is unclear. We assessed the role of sleep in inhibitory control ability with emotional stimuli, which has been shown to be suboptimal among individuals with depression and proposed to perpetuate depressive symptoms.

Methods: Emerging adults (aged 18–25 years, 64.6% female) were screened for depressive and other mental disorders by structured clinical interview and questionnaire. Individuals with depressive disorders were assigned to have a polysomnography-monitored daytime sleep opportunity (Sleep-Dep, $n = 20$), whereas nondepressed individuals were randomized to either have daytime sleep (Sleep-Ctrl, $n = 27$) or stay awake (Wake-Ctrl, $n = 18$). Participants completed the Affective Go/No-Go Task two times, separated by experimental conditions.

Results: A factorial model with a between-subject factor (Sleep-Dep/Sleep-Ctrl/Wake-Ctrl) and a within-subject factor (test 1/test 2) was used to assess if the groups differed in inhibitory control across test sessions, as inferred by changes in *d*-prime and false alarm rates (FA). Results from mixed factorial models showed a significant interaction effect between time and group on FA in the block with neutral faces as the target and happy faces as the nontarget ($F(2,61) = 5.15$, $p_{fdr} = .045$). Although Sleep-Dep had decreased FA after sleep ($t(19) = 2.94$, $p_{fdr} = .050$), Sleep-Ctrl and Wake-Ctrl had no significant between-session changes (p values $> .05$). Postsleep improvement in FA in Sleep-Dep correlated with longer stage 2 sleep ($r(20) = 0.788$, $p_{fdr} < .001$) and stage 2 fast spindle number at O1 ($r(18) = 0.692$, $p_{fdr} = .015$).

Conclusions: Sleep gain, particularly stage 2 sleep and related physiology, potentially enhances inhibitory control ability responding to emotional information among individuals with depressive disorders.

Key words: depression and anxiety, mental health, executive function, cognitive bias, information processing, nap.

INTRODUCTION

Negative bias in emotional processing is a core cognitive feature of depression (1,2). A substantial body of literature has also established the critical role that poor sleep plays in predisposing and maintaining mood disorders (3,4), although the underlying neurocognitive-affective mechanisms are unclear (5,6).

From a cognitive-behavioral perspective, depressive symptoms are perpetuated by a tendency to attend to information confirming negative beliefs and thoughts (7); depressed individuals were found to be less able to refrain from encoding negative or depressogenic information. The ability to resist distractor interference to regulate behavior in line with goals is conceived as an executive function termed *inhibitory control ability* (8). Individuals with depression were noted to have suboptimal inhibitory control ability in keeping negative information from entering and remaining in their memory system, rendering them preoccupied with mood-congruent negative information, which in turn maintains depressive symptoms (9). A recent review article suggested that negative biases and suboptimal cognitive control abilities are the main risk factors and clinical characteristics of depression (10). The Affective Go/No-Go Task (AGNG) is commonly used to measure inhibitory control ability (11,12). On the AGNG, individuals are instructed to respond to human faces of different emotional valence, such as happy faces, neutral faces, and fearful faces. The hit rate was regarded as attention

AGNG = Affective Go/No-Go Task, **DASS-D** = Depressive symptoms measured in the Depression Anxiety Stress Scale (21-item version), ***d'*** = discriminatory index, **FA** = false alarm rate, **Neu/F** = neutral face as target and fearful face as nontarget, **Neu/H block** = experimental block with neutral face as target and happy face as nontarget, **PANAS** = Positive and Negative Affect Schedule, **PSG** = polysomnography, **PSQI** = Pittsburgh Sleep Quality Index, **REM** = rapid eye movement, **SCID** = Structured Clinical Interview of the *DSM-IV-TR*, **SE** = sleep efficiency, **Sleep-Ctrl** = individuals without depressive disorders, given a daytime sleep opportunity in this study, **Sleep-Dep** = individuals with depressive disorders, given a daytime sleep opportunity in this study, **SOL** = sleep onset latency, **TST** = Total sleep time, **Wake-Ctrl** = individuals without depressive disorders who stayed awake when the other two groups had a daytime sleep opportunity in this study

SDC Supplemental Digital Content

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measures and the false alarm rate (FA) as a measure of inhibitory control (13). Previous studies using the AGNG consistently showed that individuals with depressive disorders exhibited suboptimal inhibitory control ability (11,14), which predicted the nonremission of depressive disorders (15).

Sleep problems contribute to biased emotional processing. For instance, sleep-deprived healthy adults were found to exhibit suboptimal inhibitory control ability in regulating their response toward information with affective valences, such as emotional words (16), a pattern similar to the aforementioned negative cognitive-affective bias displayed by individuals with depression (7). Functional neuroimaging studies showed that sleep problems were associated with decreased functional connectivity between frontal and limbic areas of the brain subsuming emotion regulatory processes (17,18). In a longitudinal study among 930 healthy young adults, poor sleep quality was found to prospectively predict depressive symptoms after baseline symptoms were controlled (4). Another longitudinal study among 3135 adolescents found that insufficient sleep tripled the risk of developing depression in 12 months (5). Healthy sleep is suggested to be critical to optimal brain functioning including emotion regulation, given its impact on diverse neurobehavioral processes such as inhibitory control (19). Thus far, there has only been one study that directly examined the effects of sleep on negative cognitive bias in clinical depression (20). Individuals with clinical depression showed increased intensity rating on angry face pictures after a 90-minute nap with rapid-eye-movement (REM) sleep, supporting sleep-associated altered emotional processing specific to depression.

Based on an existing theoretical model of sleep and affective functioning in nondepressed healthy adults (19), this study investigated if a daytime sleep opportunity among emerging adults with depression would alter negative cognitive bias. Emerging adulthood (age, 18–30 years) is not only a critical stage of brain development (21) but also characterized by an array of sleep difficulties (22,23) as well as mood problems, with the first major depressive episode mostly taking place during this period (24). We hypothesized that compared with their healthy counterparts, individuals with a depressive disorder would have worse inhibitory control ability over emotional information, and such inhibitory control ability would be reversed after daytime sleep. With the aim to provide pioneering data on the mechanisms of sleep impact on inhibitory control in depressed individuals, we also explored the correlational relationship between sleep physiology during the nap and postsleep changes in inhibitory control ability in the depressed group. Our study provides new information about how daytime sleep gain modulates neurocognitive-affective processing in depressed emerging adults, who are at a life stage of challenging intellectual and socioemotional demands.

MATERIALS AND METHODS

Ethics approval was obtained from the Institutional Human Research Ethics Committee from the University of Hong Kong before the commencement of the study. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the 2008 Declaration of Helsinki.

Design and Procedures

This study was part of a larger research project investigating sleep, daytime napping, and emotional functioning, which was conducted from February 2013 to March 2014. Details on sampling and recruitment procedures were described elsewhere (25). Interested participants were telephone-screened and invited to the laboratory for informed consent. Participants wore an actigraph watch and completed the sleep diary throughout the 7-day protocol, and were asked to refrain from the use of caffeine or alcohol in the 24 hours before completing the experimental session. On day 6, participants first completed state measurement at 1300 hours, followed by a neurocognitive assessment (test 1). They were then randomized to either a 90-minute polysomnography (PSG)-monitored sleep opportunity or to stay awake around 1430 to 1600 hours following a 3:1 ratio to maximize the number of participants with sleep opportunity, allowing for further investigation of individual difference factors affecting the change of performance after sleep. From 1600 to 1730 hours, research staff removed the electrodes for people who slept. All participants were encouraged to engage in quiet activities and not to be in touch with information affecting their mood. Afterward, participants completed state measurements and the posttest neurocognitive assessment (test 2) at around 1730 hours. On day 7, participants returned the actigraph watch and sleep diary, were debriefed, and obtained compensation (25).

Participants

To detect a small-medium effect size, with an α level of .05 and 80% power, 18 participants are required in each condition (25,26). Of the 305 adults expressing interest to participate in the study, 201 met the following inclusion/exclusion criteria for the larger study: no preexisting diagnosis of sleep-wake disorders, and no history of cognitive impairment or head trauma affecting cognitive functions. In addition, the Structured Clinical Interview for the *DSM-IV-TR* (SCID) (27) was used to screen the participants for this current study (see Measures for details). For the current study, 136 participants were not included because of a) presence of at least mild level of depressive symptoms without a SCID-assessed depressive disorder, or b) missing/invalid data on AGNG (n = 29), Depression Anxiety Stress Scale (DASS; n = 14), or PSG (n = 13). There were 32 participants assessed to have at least one major depressive episode or/and dysthymic disorder on the SCID, and at least mild depressive symptoms on the DASS-21 (DASS-D) >4 (28), with 20 allocated to have sleep opportunity (Sleep-Dep) and 12 to stay awake. Because of the small sample size, we did not include the 12 depressed participants in the wake condition in the current study. In the Sleep-Dep group, 15% were assessed to have a dysthymic disorder; 45%, major depressive disorder (single episode); 20%, major depressive disorder (recurrent episodes); and 20%, both dysthymic disorder and a major depressive episode. On the DASS-D, 25% had mild, 44% had moderate, 25% had severe, and 6% had very severe levels of depressive symptoms (see Measures). Although current attendance of psychiatric treatment was not an exclusion criterion, all participants confirmed no usage of any medications within the 3 months before the study period. The control group was composed of 45 participants who were assessed to have no depressive episode or dysthymic disorder on the SCID and within the normal range of depressive symptoms (DASS-D <5). Within the control group (n = 45), participants were randomized to either the sleep (Sleep-Ctrl, n = 27) or the wake condition (Wake-Ctrl, n = 18). The Wake-Ctrl group followed mostly the same procedures as the Sleep-Dep and Sleep-Ctrl groups, except that the Wake-Ctrl group stayed awake

and engaged in solitary activities under monitoring by research staff, during the period when the other two groups had the daytime sleep opportunity.

Measures

All study materials were in Chinese, and the experiments were conducted in Cantonese.

Depressive Disorders

The SCID (27) was administered by senior clinical psychology trainees supervised by a registered clinical psychologist (E.Y.Y.L.), for assessing depressive disorders and other mental disorders. The DASS-D included seven items assessing depressive symptom severity (28) and was used to further verify the depressive symptoms assessed by SCID. In the DASS-D, participants responded on a 0 to 3 scale, and scores >4, >6, >10, and >13 indicated mild, moderate, severe, and extremely severe depressive symptom levels, respectively.

Sleep Characteristics

Sleep Diary and Actigraphy

Participants were instructed to record their sleep-wake pattern for a week using a sleep diary (29). They also wore an actigraph watch (Micro Motionloggers; Ambulatory Monitoring, Inc, Ardsley, New York) on their nondominant hand throughout the study protocol as an objective measure of sleep. Actigraphic data were scored with 1-minute bins by the zero-crossing mode using Action 4 software (Ambulatory Monitoring Inc) based on a validated algorithm (30) and with reference to the sleep diary. Participants were instructed to press the event button before they went to sleep. Variables of interest included total sleep time (TST), sleep onset latency (SOL), and sleep efficiency (SE). TST was calculated by deducting SOL and wake after sleep onset from time in bed. SE was calculated as TST divided by time in bed.

Sleep Questionnaires

The Pittsburgh Sleep Quality Index (PSQI) was used to assess participants' sleep quality over seven aspects in the previous month (31,32). Poor sleepers were classified by a PSQI global score >5. The Epworth Sleepiness Scale was used to measure daytime sleepiness, with a higher score indicating a higher level of daytime sleepiness (33,34). The Composite Scale of Morningness was used to assess circadian preference, with a higher score indicating inclination toward a morningness preference (35).

PSG Recordings

Electroencephalography, electrooculography, and electromyography signals were recorded using a Compumedics E-series amplifier system (Compumedics Ltd, Abbotsford, Victoria, Australia). The electroencephalographic recording montage included frontal (F3), central (C3), and occipital (O1) electrodes referenced to A2 and a central (C4) electrode referenced to A1. A sleep technologist blind to the study objectives scored sleep stages with reference to the guidelines of the American Academy of Sleep Medicine (36). The PSG indexes included TST, SOL, wake after sleep onset, SE, and percentage of non-REM stages 1 to 4, with stage 3 and stage 4 combined as slow wave sleep, REM sleep, and REM sleep latency. For spectral analyses, spindles were identified automatically at F3, C3, and O1 during stage 2 sleep. Data were band-pass filtered from 12 to 15 Hz (slow spindles, 11–13 Hz; fast spindles, 13–15 Hz) using the one-order Butterworth IIR filters, and a spindle was detected when the root mean square of the filtered signal with a 0.1-second time window exceeded the threshold of the duration criterion of 0.5 to 3 seconds (37).

State Measurements

The Positive and Negative Affect Schedule (PANAS) was used to assess momentary positive and negative affective states (38).

Neurocognitive Assessment

The AGNG was used as it was validated among youths (13–32 years old) with neuroimaging data showing its sensitivity in activating neural substrates of inhibitory control over information with affective valence (39,40). Participants completed six blocks of AGNG with fearful, happy, and neutral faces, one as target and another one as nontarget in each block (41). Each stimulus was presented for 500 milliseconds about eight times as either target or nontarget in the six blocks in a pseudorandom order. Participants were instructed to press a button as quickly as possible when target faces were presented and to withhold response for other expressions (nontargets). Reaction time and accuracy were measured. Discriminatory index (d') was calculated based on the signal detection theory (42), and a higher level of d' indicated better overall task performance. In addition, lower hit rates reflected worse attention, and higher FA rates reflected worse inhibitory control ability (13). Attention and processing speed were measured by the 0-back condition of the N-back spatial task and the computerized Trail Making Test—Part A (TMT-A) to control for any baseline group differences in basic cognitive functions (43–45).

Statistical Analyses

The difference between the Sleep-Dep, Sleep-Ctrl, and Wake-Ctrl groups on demographics, basic cognitive functions, and sleep and affect variables were tested with one-way analysis of variance and χ^2 tests. Internal consistency of self-reported questionnaire is studied by Cronbach α. A mixed factorial model with a within-subject factor, time (time 1/time 2) and between-subject factor, group (Sleep-Dep/Sleep-Ctrl/Wake-Ctrl), was used to study the impact of daytime sleep on the group's inhibitory control ability. For the exploratory research aim, given the expected high true correlation between test 1 and test 2 measures (46) and the usual practice in the napping paradigm (47), we computed performance change scores across sessions by subtracting test 2 from test 1 performance. Improved performance is indicated by negative change scores of hit rate and d' on AGNG and PANAS ratings, and positive change scores of FA on AGNG. Change scores were correlated with PSG indexes. The Benjamini-Hochberg procedure with a false discovery rate of 0.05 was used to adjust for multiple comparisons (48).

RESULTS

Group Characteristics

Between-group differences in demographics, sleep patterns, and basic cognitive functions are presented in Table 1. The groups were significantly different on the PSQI global score ($F(2,64) = 7.16, p = .002$) but not on any other sleep measures (p values > .05; Table 1). Post hoc analysis (least significant difference [LSD])

TABLE 1. Demographic, Baseline Sleep, and Mood Variables

	Wake-Ctrl	Sleep-Ctrl	Sleep-Dep	F or χ^2	p	Cronbach α
n	18	27	20			
Age, y	19.9 (1.8)	20.2 (1.3)	20.8 (1.9)	0.398	.26	
Sex, % female	55.6	66.7	70.0	0.950	.62	
Body mass index, kg/m^2	19.3 (2.7)	19.4 (2.0)	19.9 (3.4)	0.259	.77	
TST, 7 d, h	7.7 (0.7)	7.5 (1.1)	7.2 (0.9)	1.197	.31	
SE, 7 d, %	97.7 (1.6)	97.3 (1.7)	97.8 (1.3)	0.653	.52	
SOL, 7 d, min	6.0 (7.5)	2.4 (2.8)	4.7 (5.4)	2.622	.081	
WASO, 7 d, min	11.1 (8.4)	12.2 (7.4)	10.0 (6.3)	0.499	.61	
ESS	11.1 (3.9)	11.4 (4.0)	11.5 (4.4)	0.050	.95	.742
PSQI[a]	6.2 (2.5)	4.8 (2.3)	7.6 (2.8)	7.161	.002	.530
CSM	27.8 (5.7)	29.4 (5.0)	29.6 (6.4)	0.598	.55	.761
DASS, depression[b]	2.1 (1.5)	1.3 (1.3)	9.0 (3.0)	87.441	<.001	.867
TMT-A, accuracy	0.91 (.08)	0.91 (0.09)	0.92 (0.09)	0.102	.90	
0-Back, accuracy	0.92 (0.09)	0.93 (0.06)	0.93 (0.05)	0.075	.93	

Values are means (standard deviations). χ^2 Test was used to compare the sex distribution between groups, and other group differences were tested by one-way analysis of variance.

Wake-Ctrl = individuals without depressive disorders who stayed awake when the other two groups had a daytime sleep opportunity in this study; Sleep-Ctrl = individuals without depressive disorders, given a daytime sleep opportunity in this study; Sleep-Dep = individuals with depressive disorders, given a daytime sleep opportunity in this study; TST = total sleep time; SE = sleep efficiency; SOL = sleep onset latency; WASO = wake after sleep onset; ESS = Epworth Sleepiness Scale; PSQI = Pittsburgh Sleep Quality Index; CSM = Composite Scale of Morningness; DASS = Depression Anxiety Stress Scale; TMT = Trail Making Test; 0-Back = 0-back condition of the N-back spatial task.

[a] Post hoc analyses (LSD) showed that the Sleep-Dep had poorer sleep quality than the Sleep-Ctrl (mean difference = −2.79, $p < .001$) but was not significantly different from the Wake-Ctrl (mean difference = −1.43, $p = .082$).

[b] Post hoc analyses (LSD) showed that the Sleep-Dep had significantly more severe depressive symptoms than the Sleep-Ctrl (mean difference = −7.67, $p < .001$) and Wake-Ctrl (mean difference = −6.94, $p < .001$).

showed that the Sleep-Dep had poorer sleep quality than the Sleep-Ctrl (mean difference = −2.79, $p < .001$), but was not significantly different from the Wake-Ctrl (mean difference = −1.43, $p = .082$). The groups were significantly different on PANAS negative affect ($F(2,64) = 9.97$, $p < .001$) but not on PANAS positive affect ($F(2, 64) = 1.40$, $p = .25$). Post hoc analysis (LSD) showed that the Sleep-Dep had more negative affect than the Sleep-Ctrl (mean difference = −5.80, $p < .001$) and Wake-Ctrl (mean difference = −5.09, $p = .001$). The Sleep-Dep and Sleep-Ctrl were not significantly different on their sleep characteristics measured by PSG during the nap (Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A775). There were also no significant effects of time or group or their interaction on the basic cognitive functions measure by the 0-back condition of the N-back spatial task and the Trail Making Test Part A (Table S2, Supplemental Digital Content, http://links.lww.com/PSYMED/A775).

Effects of Sleep on Affective States and Inhibitory Control

Results from the mixed factorial model showed a significant interaction effect of group with time on PANAS positive affect ($F(2,61) = 8.48$, $p_{fdr} = .010$, $\eta_p^2 = 0.22$; Table 2). Follow-up analyses showed that after the daytime sleep, the Sleep-Dep had a more positive affect ($t(19) = -2.70$, $p_{fdr} = .042$), the Sleep-Ctrl had no significant change ($t(25) = 1.45$, $p_{fdr} = .16$), and the Wake-Ctrl had a marginally significant decrease in positive affect at session 2 ($t(17) = 2.76$, $p_{fdr} = .053$; Figure S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A775). For negative affect, there was no significant interaction effect ($F(2,61) = 3.12$, $p = .051$), but a significant main effect of time ($F(1,61) = 68.07$, $p_{fdr} < .001$, $\eta_p^2 = .53$), in which all participants had decreased negative affect in session 2, and a significant main effect of group ($F(2,61) = 12.67$, $p_{fdr} < .001$, $\eta_p^2 = .29$), with post-hoc analyses (LSD) indicating the Sleep-Dep group had a significantly higher level of PANAS negative affect than the Sleep-Ctrl (mean difference = 4.85, $p_{fdr} < .001$) and the Wake-Ctrl group (mean difference = 4.38, $p_{fdr} < .001$; Figure S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A775).

For inhibitory control, on the blocks with fearful face as target, there was a significant main effect of time on FA ($F(1,61) = 7.96$, $p_{fdr} = .037$, $\eta_p^2 = 0.12$), with no group or interaction effects (p values > .05; Table 2), suggesting that all groups had increased FA at test 2. There were no significant main or interaction effects with hit rate or d' as the outcome for fearful face and no significant effects on any outcome measures with happy face as target (Table 2). On the blocks with happy face as target, there was no significant main or interaction effect (p values > .05; Table 2). On the blocks with neutral face as target, there was a significant main effect of group on hit rate ($F(2,61) = 8.04$, $p_{fdr} = .008$, $\eta_p^2 = 0.21$), with nonsignificant main effect of time or interaction effect (Table 2). There were significant interaction effects between time and group on d' ($F(2,61) = 8.23$, $p_{fdr} = .009$, $\eta_p^2 = 0.21$) and FA ($F(2,61) = 6.45$, $p_{fdr} = .018$, $\eta_p^2 = 0.18$), whereas the main effects of group and time were both nonsignificant (p values > .05; Table 2).

With the significant interaction effects observed in the blocks with neutral face as target, we proceeded to investigate whether the result pattern effect is different between the block with happy face or fearful face as nontarget. On the block with neutral face as target and fearful face as nontarget (Neu/F), we observed no significant main or interaction effects on the d', FA, or hit rate (p values > .05; Table 2). On the block with neutral face as target with happy face as nontarget (Neu/H block), there was a significant

TABLE 2. Mixed Factorial Model Results on Affective States and Inhibitory Control Measures

	Wake-Ctrl (n = 18)		Sleep-Ctrl (n = 27)		Sleep-Dep (n = 20)		F		
	T1	T2	T1	T2	T1	T2	Grp	Time	Int
Pos affect	27 (6.0)	24 (6.6)	28 (6.6)	26 (7.0)	25 (6.3)	28 (6.5)	0.278	0.338	8.48[a]
Neg affect	15 (5.6)	11 (2.4)	14 (2.9)	11 (2.1)	20 (5.3)	15 (3.7)	12.67[a]	68.07[a]	3.12
Hap *d*	0.91 (0.08)	0.88 (0.07)	0.90 (0.07)	0.91 (0.06)	0.88 (0.07)	0.88 (0.10)	1.31	1.23	1.39
Hap H	1.0 (0.01)	1.0 (0.01)	1.0 (0.00)	1.0 (0.00)	1.0 (0.00)	1.0 (0.01)	0.422	0.068	1.82
Hap F	0.09 (0.08)	0.12 (0.07)	0.09 (0.07)	0.09 (0.06)	0.12 (0.07)	0.12 (0.10)	1.26	1.33	1.42
Fear *d*	0.87 (0.08)	0.84 (0.07)	0.86 (0.08)	0.86 (0.07)	0.85 (0.08)	0.80 (0.12)	1.14	4.84[b]	0.861
Fear H	0.99 (0.01)	0.99 (0.02)	0.98 (0.04)	1.0 (0.01)	0.98 (0.04)	0.99 (0.01)	0.141	1.66	0.871
Fear F	0.12 (0.08)	0.15 (0.08)	0.12 (0.07)	0.14 (0.07)	0.13 (0.07)	0.18 (0.12)	0.998	7.96[a]	0.872
Neu *d*	0.87 (0.09)	0.84 (0.08)	0.89 (0.07)	0.86 (0.07)	0.81 (0.13)	0.86 (0.09)	1.55	0.88	8.23[a]
Neu H	1.0 (0.01)	1.0 (0.1)	1.0 (0.01)	1.0 (0.00)	0.98 (0.03)	0.99 (0.01)	8.04[a]	3.91	2.38
Neu F	0.12 (0.08)	0.16 (0.08)	0.11 (0.07)	0.14 (0.07)	0.17 (0.11)	0.13 (0.09)	0.967	0.856	6.49[a]
N/H *d*	0.89 (0.10)	0.84 (0.07)	0.90 (0.09)	0.86 (0.10)	0.80 (0.14)	0.87 (0.10)	1.60	0.139	7.16[a]
N/H H	1.0 (0.01)	1.0 (0.01)	1.0 (0.01)	1.0 (0.01)	0.97 (0.06)	0.99 (0.02)	6.61[a]	2.22	1.87
N/H F	0.11 (0.10)	0.15 (0.07)	0.10 (0.09)	0.14 (0.10)	0.17 (0.11)	0.12 (0.10)	0.634	0.872	5.15[a]
N/F *d*	0.85 (0.12)	0.83 (0.12)	0.88 (0.07)	0.87 (0.09)	0.82 (0.14)	0.85 (0.09)	1.12	0.001	2.18
N/F H	1.0 (0.01)	0.99 (0.02)	0.99 (0.01)	1.0 (0.01)	0.99 (0.02)	0.99 (0.02)	1.07	1.94	0.933
N/F F	0.14 (0.12)	0.16 (0.11)	0.11 (0.07)	0.13 (0.09)	0.17 (0.13)	0.14 (0.09)	0.986	0.129	1.833

Values are means (standard deviations).

Wake-Ctrl = individuals without depressive disorders who stayed awake when the other two groups had a daytime sleep opportunity in this study; Sleep-Ctrl = individuals without depressive disorders, given a daytime sleep opportunity in this study; Sleep-Dep = individuals with depressive disorders, given a daytime sleep opportunity in this study; Grp = group; Int = interaction; Pos/Neg = positive/negative affect in the Positive and Negative Affect Scale; *d* = discriminatory index; H = hit rate; F = false alarm rate; Hap/Fear/Neu = mean performance in experimental blocks with happy/fear/neutral faces as targets and the other two type of faces as nontargets; N/H = block with neutral face as target and happy face as nontarget; N/F = block with neutral face as target and fearful face as nontarget.

[a] p Value remained significant after adjustment for false discovery rate.

[b] p Value became nonsignificant after adjustment for false discovery rate.

main effect of group on hit rate ($F(2, 61) = 6.61$, $p_{fdr} = .018$, $\eta_p^2 = 0.18$). Post hoc analysis (LSD) showed that the Sleep-Dep had a significantly lower hit rate than the Sleep-Ctrl (mean difference = −0.02, $p_{fdr} = .048$) and Wake-Ctrl (mean difference = −0.02, $p_{fdr} = .045$), whereas the Sleep-Ctrl and Wake-Ctrl were not significantly different from each other (mean difference = 0.0001, $p_{fdr} > .05$; Table 2). For the models with d' ($F(2,61) = 7.16$, $p_{fdr} = .014$, $\eta_p^2 = 0.19$) and FA ($F(2,61) = 5.15$, $p_{fdr} = .045$, $\eta_p^2 = 0.14$) as outcomes, there was a significant interaction effect of time with group, with no significant main effects (p values > .05; Table 2). Follow-up analyses showed that, although Sleep-Dep had increased d' ($t(19) = -3.03$, $p_{fdr} = .044$) and decreased FA ($t(19) = 2.94$, $p_{fdr} = .050$), no significant changes on d' ($t(25) = 1.85$, $p = .19$) or FA ($t(25) = -1.90$, $p = .070$)were found in the Sleep-Ctrl, or d' ($t(17) = 1.83$, $p = .084$) or FA ($t(17) = -1.51$, $p = .15$) in the Wake-Ctrl (Figure 1).

Sleep Physiology and Performance Change After Sleep in Depressed Group

Among the Sleep-Dep, we found the decrease of FA in Neu/H to correlate with more stage 2 sleep ($r(20) = 0.788$, $p_{fdr} < .001$; Figure 2), whereas change scores on positive affects did not correlate with any PSG indexes (Table S3, Supplemental Digital Content, http://links.lww.com/PSYMED/A775). We proceeded to explore if the decrease of FA in Neu/H was related to stage 2 sleep spindle number and density at F3, C3, or O1. The decrease of FA in Neu/H significantly correlated with fast sleep spindle detected at O1 ($r(18) = 0.692$, $p_{fdr} = .015$; Figure 3). In addition, the change in FA of Neu/H did not correlate with change in positive affects, suggesting independent factors underlying the changes. For completeness, we correlated PSG indexes with Neu/H FA in the Sleep-CTRL group and found no statistically significant correlations (p values > .05).

DISCUSSION

Our findings supported the hypotheses that individuals with depressive disorders exhibited worse performance in inhibiting their response toward emotional information, particularly in differentiating positive from neutral information and that following a daytime sleep opportunity, such suboptimal inhibitory control ability over positive information of the depressed individuals returned to a level comparable to the nondepressed controls with or without daytime sleep. The misidentification of happy faces as neutral faces and the resulting failure to inhibit their responses might reflect a depressogenic cognitive error characterized by a tendency to discount positive information (e.g., positive facial expression) as neutral or nonpositive (49). One potential explanation of the finding is that individuals with depression tend to have a hyperactivated amygdala (19,50), leading to heightened reactivity to emotional stimuli. The modulating effect of daytime sleep on cognitive bias might be related to the sleep-specific neurochemical state that facilitates optimal functional connectivity of the cortical and subcortical networks subserving cognitive-affective processing

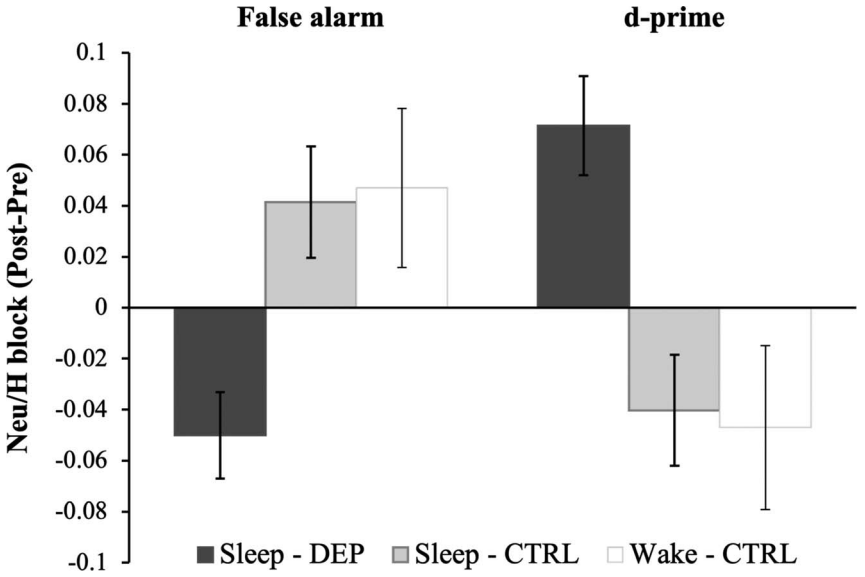

FIGURE 1. Group difference on false alarm rate and d' in blocks with neutral face as target and happy face as nontarget, after daytime sleep. Positive score indicated increase on false alarm or d' across sessions. Ctrl = control group; Dep = depression group. Error bars represent standard error.

(51). For instance, previous studies found that daytime sleep specifically benefited consolidation of emotional but not neutral memories (52–54). Another plausible explanation of the improved performance might be related to the sleep-dependent reversal of compromised basic neuropsychological functions in depressed individuals, such as lowered energy level, memory, concentration, and attention ability (24,55), which typically improve after napping in healthy populations (56). However, we observed a nonsignificant group by time interaction effect on attention and processing speed in our sample, hence discounting such explanation.

A recent study found that, although a REM-containing nap increased perceived intensity rating on angry faces exclusively in depressed individuals, a non-REM nap seemed to reduce the intensity of perception of sad faces for the depressed participants (20). The current study revealed a beneficial napping effect independent from REM on inhibitory control in processing happy

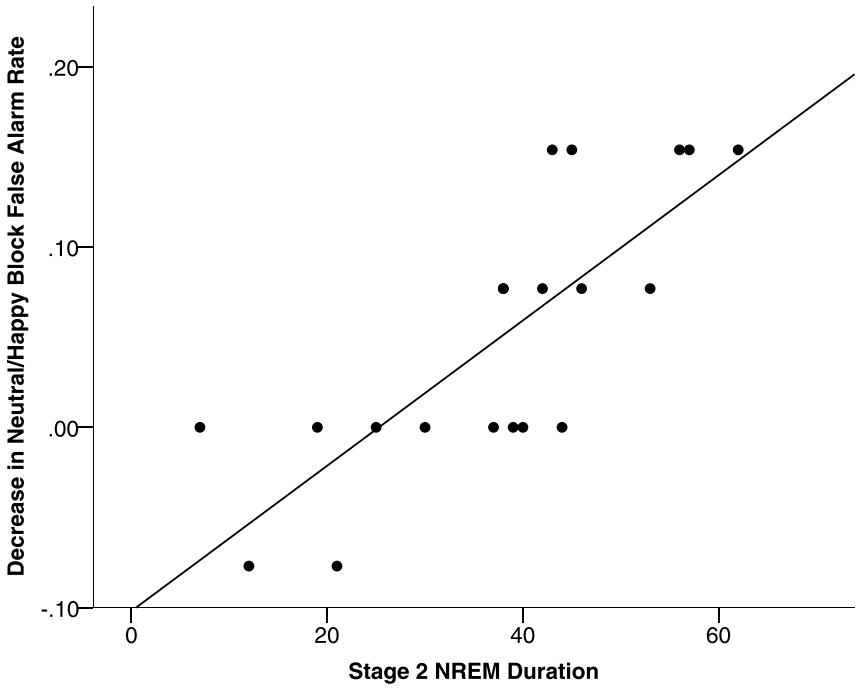

FIGURE 2. Decreased false alarm rate in block with neutral face as target and happy face as nontarget was significantly correlated with S2 duration after false discovery rate adjustment ($r(20) = 0.788$, $p < .001$). Neu/H block = experimental block with neutral face as target and happy face as nontarget; NREM = nonrapid eye movement.

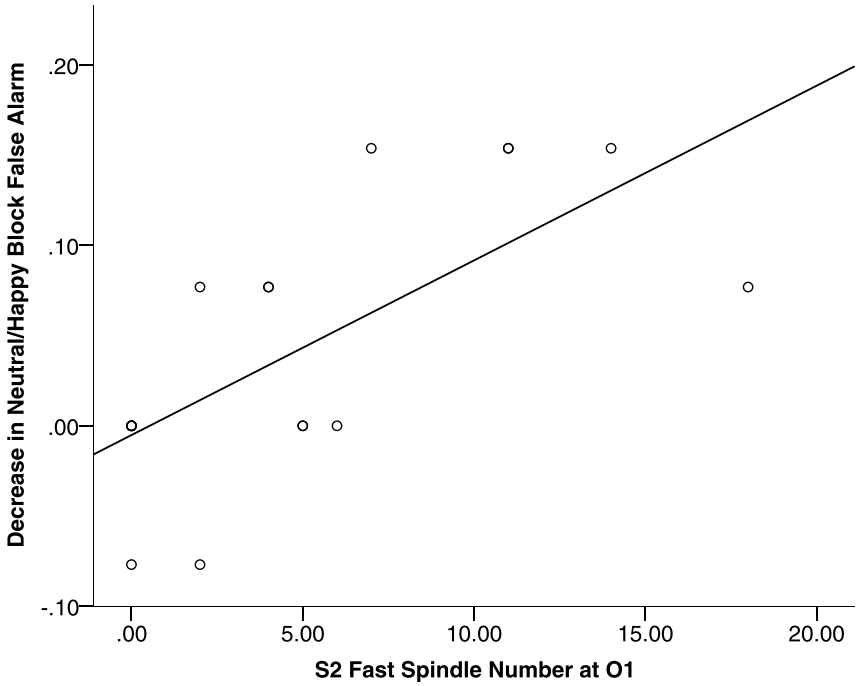

FIGURE 3. Decreased false alarm rate in block with neutral face as target and happy face as nontarget was significantly correlated with more S2 fast spindle detected at O1 after false discovery rate adjustment ($r(18) = 0.692$, $p = .001$).

faces more accurately, also exclusively in depressed individuals. The amount, proportion, or latency of REM did not correlate with postnap changes in inhibitory control in this study. Furthermore, although both perception and inhibitory control of emotional information might be functionally related, they are subserved by different neural networks (12,19,20,57), which could be differentially affected by sleep. Taken together, evidence thus far seems to suggest that sleep-related depressogenic effects on affective processing might be specific to REM sleep and that non-REM napping might mitigate certain cognitive-affective biases observed in depressed individuals. Future studies assessing various depression-associated affective processes with a napping paradigm of conditions with and without REM would be helpful in delineating the heterogenous effects of napping in emotional processing.

Improvement in Neu/H FA was positively related to stage 2 sleep and stage 2 fast sleep spindles detected at O1 in the depressed group. Although the scarce napping PSG data in depressed individuals published thus far have not demonstrated a functional role of stage 2 sleep or spindles originated from the occipital lobe, our findings could be interpreted in light of existing understanding of the associations of sleep spindles and occipital regions with the consolidation of learning (58). During stage 2 sleep, there is increased functional connectivity of the hippocampus and other subcortical regions with the neocortex, subserving consolidation of learned information into long-term memory (59–61). Although the current experimental task, AGNG, requires visual attention and inhibitory control ability (62), it is conceivable that stage 2 fast spindle detected at the occipital region supports acquisition, processing, and consolidation of visual materials (63), which in turn enhance inhibitory control in visual processing underlying cognitive-affective biases. Relatedly, after one night of sleep deprivation and 8 hours of recovery sleep, young adults' metabolism in both frontal and occipital lobes were correlated with visual attention and inhibitory control (64), supporting the role of sleep in inhibitory control modulated by frontal and occipital structures and the potential function of the occipital lobe in compensating for frontal dysfunctions after sleep loss in healthy individuals. With the well-documented aberrations of the functional networks particularly involving the frontal areas characterizing depressive disorders in adults (65) and in youths (66), our results on occipital sleep spindle might represent a compensatory mechanism of the posterior lobe for the frontal dysfunctions behaviorally observed in depressed individuals (67), as in the sleep-deprived young adults (64).

Limitations

First, the absence of overnight PSG data precluded further understanding of the potential moderating effects of nighttime sleep features in influencing the impact of daytime napping on performance. Second, we had a sample of unmedicated and highly educated college students constraining the generalizability to other populations. Besides, our depressed group had a rather wide variability of depressive symptom severity and disorder subtype. Although the variability may reflect the clinical heterogeneity in depressive symptomatology and the rate of depression (10%) among our sample is comparable to the prevalence reported in the general public (7.6%–12.9%) (68,69) or college students (4%–15.7%) (70,71), the nonspecificity of the sample may render it difficult to ascertain to which populations our findings may apply. Future work could consider examining whether patient subgroups and subclinical populations perform differentially in terms of their cognitive-affective functions under sleep manipulations. Third, we only had a small number of depressed individuals randomized to wake condition ($n = 12$), which was excluded from the analyses because of low statistical power. Such lack of a depression wake-control group constrains the understanding of whether cognitive bias changes across the day without a daytime nap in depressed individuals. Fourth,

the between-session changes might arguably be influenced by factors other than daytime sleep, such as practice effect or circadian influence over functional performance (72). Nevertheless, our sessions took place from early to late afternoon uniformly across participants, but improved inhibitory control was only observed in the SleepDep group, countering the arguments for between-session changes being driven by general practice effect or circadian factors.

In conclusion, although depression is among the top causes for the burden of disease in the world (73), this study provides novel evidence that an additional sleep opportunity potentially brings therapeutic effects on depressed youths' affect and their ability to inhibit behavioral responses consistent with their negative cognitive bias to emotional stimuli. Such knowledge helps inform the development of sleep-focused interventions targeting cognitive-affective functioning for individuals with mood disturbances and preventative sleep health education for emerging adults who are at high risk for both sleep and mood disruptions.

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