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ORIGINAL ARTICLE

Neural response to rewards in youths with insomnia

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Abstract

Study Objectives: Insomnia and depression are common comorbid conditions in youths. Emerging evidence suggests that disrupted reward processing may be implicated in the association between insomnia and the increased risk for depression. Reduced reward positivity (RewP) as measured by event-related potential (ERP) has been linked to depression, but has not been tested in youths with insomnia.

Methods: Twenty-eight participants with insomnia disorder and without any comorbid psychiatric disorders and 29 healthy sleepers aged between 15–24 completed a monetary reward task, the Cued Door task, while electroencephalographic activity was recorded. RewP (reward minus non-reward difference waves) was calculated as the mean amplitudes within 200–300 ms time window at FCz. Two analyses of covariance (ANCOVAs) were conducted with age as a covariate on RewP amplitude and latency, respectively.

Results: Participants with insomnia had a significantly lower RewP amplitude regardless of cue types (Gain, Control, and Loss) than healthy sleepers, $F(1, 51) = 4.95$, $p = 0.031$, indicating blunted reward processing. On the behavioral level, healthy sleepers were more prudential (slower reaction time) in decision making towards Loss/Gain cues than their insomnia counterparts. Trial-by-trial behavioral adjustment analyses showed that, compared with healthy sleepers, participants with insomnia were less likely to dynamically change their choices in response to Loss cues.

Conclusions: Dysfunctional reward processing, coupled with inflexibility of behavioral adjustment in decision-making, is associated with insomnia disorder among youth, independent of mood disorders. Future studies with long-term follow-up are needed to further delineate the developmental trajectory of insomnia-related reward dysfunctions in youth.

Statement of Significance

This study found blunted reward responsiveness and a lack of reward-dependent behavioral adjustment in youths with primary insomnia disorder. These findings highlighted altered reward functioning in the context of insomnia and suggested the need for enhanced clinical attention to potential reward dysfunction-related psychopathology in insomnia.

Key words: reward processing; insomnia; youth; adolescent; electroencephalography

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Introduction

Insomnia is the most common sleep problem in youth, especially in late adolescence, with a prevalence ranging from 34% to 69% [1–6]. Insomnia has been shown to be associated with an increased risk of developing psychiatric disorders, interpersonal difficulties, somatic health problems, self-harm and suicidal ideation in youth [4, 7–11]. In particular, insomnia often precedes or is comorbid with depression [12, 13]. A community-based longitudinal study conducted in youths aged 11–17 suggested a reciprocal relationship between depression and insomnia, such that baseline insomnia increased the likelihood of subsequent depression by two-fold at one-year follow-up, and vice versa [14]. Meanwhile, treatment targeting insomnia has been shown to improve not only sleep but also depressive symptoms in insomnia patients with comorbid depression [15], including among adolescents [16, 17]. There is also emerging evidence that the treatment for insomnia may prevent the development of depression [18, 19].

Despite the close link between insomnia and depression, the mechanism underlying their association remained elusive, with the possibility of involving neurobiological, psychological, and social factors [20–22]. Among various factors, impaired reward processing has been shown to be associated with both depression and insomnia. Reward processing includes multiple psychological processes, such as learning contingencies between actions and rewarding outcomes, the experiences of pleasure upon receipt of rewarding stimuli (i.e. liking), and the motivation to approach/obtain rewards (i.e. wanting) [23, 24]. Deficits in reward processing has been linked to anhedonia, characterized by a lack of positive affect, which is a core feature of depression [25]. Blunted activation of the fronto-striatal reward network, which is known to play a significant role in reward processing, has also been found among individuals with depression [26]. Prior evidence showed that reduced processing upon receiving rewards preceded and predicted the onset of depression [27–29], and it was suggested as one central vulnerability factor underlying depression [30, 31]. Growing evidence also suggested blunted reward processing as one potential mechanism linking insomnia and depression in youth [20, 22, 26]. Reward processing is especially important in the context of youth development due to immaturities in the reward and motivation systems of the forebrain circuits in adolescence [32, 33]. Specifically, blunted reward response as measured by event-related potentials (ERPs), that is, the reduced reward positivity or RewP, was found to interact with self-reported poor sleep (as measured by the Pittsburgh Sleep Quality Index; PSQI) in increasing the risk of developing depressive symptoms among 8–14 years old adolescent girls during one-year follow-up [34]. Another longitudinal fMRI study conducted in the adolescent girls found that reward response in the dorsal medial prefrontal cortex (dmPFC; measured at age 16) mediated the relationship between insomnia symptoms in early adolescence (age 9–13) and depressive symptoms in late adolescence (age 16–17) [35]. Although both studies demonstrated a close interplay between sleep and reward functioning in predicting depression, it remained unclear whether reward dysfunction might be associated with insomnia disorder independent of mood disorders. There has been some preliminary evidence that sleep disruption per se (e.g. short sleep duration as measured by actigraphy and poor sleep quality by self-report) could be associated with reward processing deficits in healthy adolescents without psychiatric disorders [36]. Nonetheless, whether insomnia disorder affects reward processing, especially in youths who may be particularly vulnerable to the risk of developing mood disorders, awaits further investigation.

To address the existing research gaps, this study set out to investigate whether insomnia disorder would be associated with blunted reward processing in adolescents and young adults. To our knowledge, this is the first study that investigated reward processing in insomnia disorder using reward positivity (RewP), which reflects the variability in the event-related potential following gain versus loss feedback during a monetary reward paradigm (i.e. the Cued Doors task). We hypothesized that non-depressed youths with insomnia disorder would demonstrate blunted neural response to reward as compared to their healthy sleeper counterparts.

Methods

Participants

Youths aged between 15 and 24 years with insomnia disorder and their healthy sleeper counterparts were recruited to take part in this study. We chose the age range of 15–25 to cover a wider developmental span, derived from the definition of youth by World Health Organization [37]. Participants meeting the following criteria were included in the insomnia group: (1) meeting the diagnostic criteria of insomnia disorder according to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) diagnostic criteria of insomnia disorder (including all of the following criteria: having at least one of the sleep difficulties including difficulty initiating sleep, difficulty maintaining sleep, or early-morning awakening, with inability to return to sleep; experiencing sleep difficulties for at least three nights per week despite adequate opportunity for sleep; having sleep difficulties for at least 3 months; having sleep difficulties not due to any coexisting sleep-wake disorders, mental disorders, or medical conditions; and experiencing significant functional impairment or distress) [38]; and (2) having a score on Insomnia Severity Index (ISI) ≥9, the suggested cut-off score for adolescents [39]. Healthy youth participants who were free of any sleep and psychiatric disorders were recruited as the controls. Exclusion criteria of the study included: night-shift workers, a current diagnosis of any neuropsychiatric or sleep disorder (other than insomnia for the insomnia group) as confirmed by the clinical interview, current use of medications or having any prominent medical condition affecting sleep or cognition, or impaired vision and hearing deficit.

Procedures

Participants were recruited via mass emails, online advertisement, posters and flyers in the local community. To ascertain one's eligibility for this study, potential participants who expressed interest in taking part in this research underwent a screening session using two validated semi-structured clinical interviews: Diagnostic Interview for Sleep Patterns and Disorder (DISP) to rule out major sleep disorders, such as narcolepsy, restless leg syndrome, obstructive sleep apnea, and parasomnias [40, 41], and Mini-International Neuropsychiatric Interview (MINI) [42] to screen for psychiatric disorders, such

as major depression, anxiety disorders, and psychotic disorders [43, 44]. Eligible participants completed a battery of self-report questionnaires, and were instructed to complete a daily sleep diary whilst wearing a wrist actigraphy (Actiwatch Spectrum PRO, Philips—Respironics) to measure their sleep at home for seven consecutive days before the EEG experiment. To eliminate time-of-the-day effect, all the EEG experiments were scheduled from 10:30 am to 12:30 pm, except for four participants (n = 2 in insomnia group, rescheduled to start from 2:30 pm or 3:30 pm). Written informed consent forms were signed by all the participants, whilst parent/guardian consent forms were additionally collected from those aged below 18. The study protocol was approved by the Institutional Ethics Committee. Participants who completed the study were given HKD$400 cash as remuneration.

Measures

Subjective sleep and mood measures. Insomnia Severity Index (ISI) [45] is a 7-item scale to measure different symptom dimensions of insomnia (e.g. problems with sleep onset, sleep maintenance, and early morning awakening). ISI has been shown to be a reliable and valid instrument for measuring insomnia in Chinese adolescents [39]. An ISI score ≥9 is considered as a cut-off score suggestive of the presence of clinical insomnia in adolescents (87% sensitivity and 75% specificity) [39]. Pittsburgh Sleep Quality Index (PSQI) [46] is a 19-item scale to assess self-reported sleep quality, which has been validated in the Chinese population (Cronbach's α = 0.83) [47, 48]. Chronotype preference was measured by the Chinese version of the Reduced Morningness/Eveningness Questionnaire (rMEQ; Cronbach's α = 0.84) [49, 50]. The Chinese version of the Hospital Anxiety and Depression Scale (HADS) [51], which consists of a 7-item anxiety subscale (HADS-A; Cronbach's α = 0.83) and a 7-item depression subscale (HADS-D; Cronbach's α = 0.82), has been established as a useful screening and assessment instrument for anxiety and depression in the general population [52]. The Depressive Symptom Inventory Suicidality Subscale (DSI-SS; Cronbach's α = 0.90) is a 4-item self-report questionnaire designed to assess the frequency and severity of suicidal ideation in the past 2 weeks [53, 54].

Objective sleep measure. Actigraphy (Philips Respironics, Murrysville, PA) was used to objectively measure sleep. Actigraph was configured to record in 1-min epochs. When scoring actigraphy data in Actiware software, we determined and set the rest interval using the inputs in the following order of importance: (1) event marker, (2) sleep diary, (3) white light intensity, (4) activity level, with reference to a previous study [55]. Sleep parameters generated for the analysis included total sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO), and sleep efficiency (SE).

Experimental paradigm. In this study, we assessed reward processing by examining the consumption of rewards (i.e. liking) when people receive monetary rewards. We used the Door Task to assess reward sensitivity (programmed in E-Prime 2.0, see Figure 1 for the task procedure). Before the task, participants were told that they would receive actual monetary reward based on their accuracy of guessing which of the two doors contained a reward behind. There were three types of Cues: Gain cue; Loss cue; No-gain No-loss/Control cue. After participants entered their guess by pressing either the left or the right button on the keyboard, they were presented with either a green arrow (reward) or a red arrow (non-reward). Participants

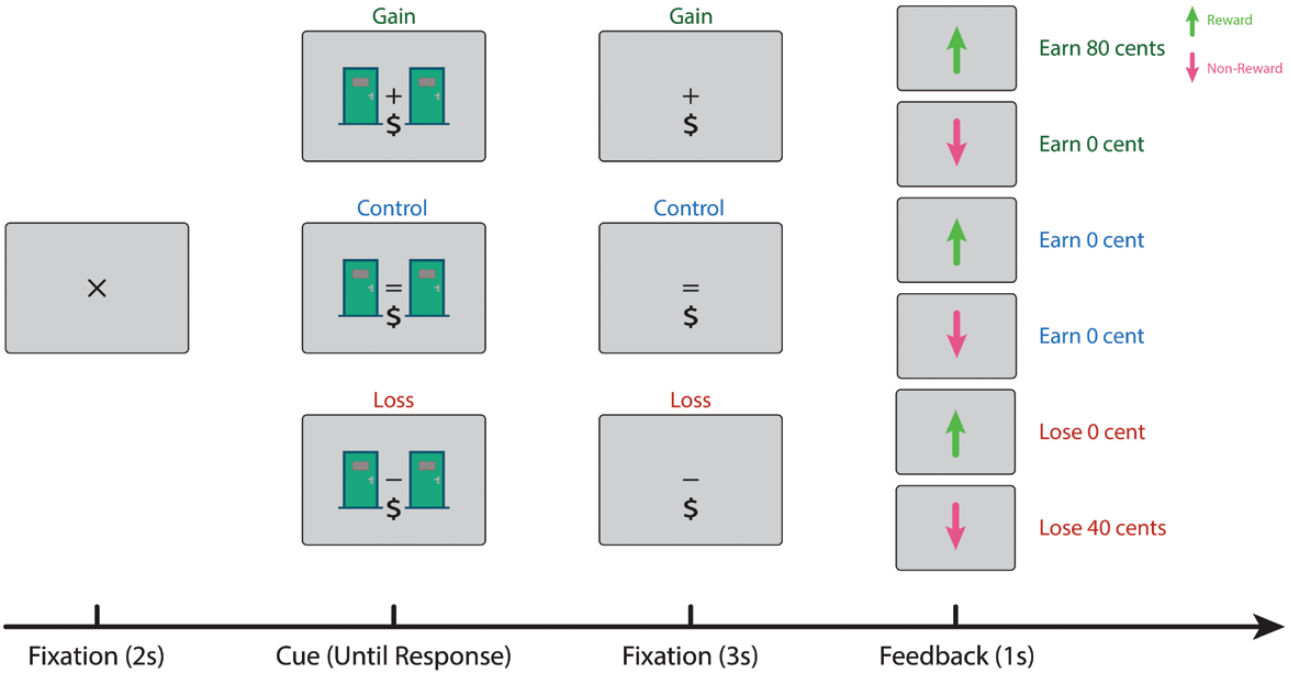

Figure 1. Demonstration of the door task. The first screen of each trial was presented with the central fixation cross. The second screen showed an image of two doors, with a 'Cue' sign in between the two doors. The cue signs indicated the condition of the present trial (Gain cue: '+$' sign; No-gain No-loss, control cue: '=$' sign; Loss cue: '-$'sign). Participants were instructed to guess which door has a monetary prize behind it by pressing either the left or right button on the keyboard. Next, participants were given feedback after each guess response (green arrow indicating reward, and red arrow indicating non-reward).

were informed that they would gain 80 cents in the Gain cue condition upon seeing the green arrow, they would lose 40 cents in the Loss cue condition upon seeing the red arrow, and they would neither gain nor lose any money in the Control cue condition. Participants first completed a practice block containing six trials (3 Types of Cues × 2 Feedback), followed by the main task consisting of 180 trials (30 trials in each of the 6 conditions) equally divided into 18 blocks. Each trial started with a 2-second fixation cross, followed by the cue presentation ("+" for Gain, "–" for Loss, and "=" for Control; see Figure 1). Participants were also prompted to guess whether the left or right door contained the reward (vs. non-reward) and they were encouraged to maximize their earnings. Participants' responses and reaction times (RTs) associated with each trial were recorded for behavioral analyses. After participants made a response, the cue remained on the screen for another 3 s as a fixation, before the green-upward arrow (reward) or the red-downward arrow (non-reward) was presented. During the breaks, the accumulated money gained by the participants would appear on the computer screen. Unbeknown to the participants, the task was pre-programmed so that all the participants would receive the same feedback throughout the task and would gain 1,200 cents (as shown on the screen) at the end of the study regardless of their guessing performance. After finishing all the testing blocks, participants were asked to estimate the probabilities of reward for each type of cue, which yielded part of the behavioral outcomes of this task. In the end, participants were debriefed and rewarded with HKD$12 in cash upon completing the experiment.

To examine the trial-by-trial behavioral adjustment across three conditions, that is, whether a previous loss-cue trial would motivate participants to change their choices in the following trial, we used Previous trial response (left vs. right button), Cue type (Gain vs. Control vs. Loss), Group (insomnia vs. healthy sleeper), and their interactions as predictors in a linear mixed effects model to predict participants' next trial's response (left vs. right). For random effect, we modeled random intercepts for each participant. Trials were excluded if reaction time was longer than mean plus three standard deviations (*SD*s) or <300 ms within each participant.

Reaction times (RTs) were investigated in a linear mixed effects model with cue type (Gain vs. Control vs. Loss), group (insomnia vs. healthy sleeper), and their interaction as predictors. Trials with RTs that were longer than mean plus three *SD*s or <300 ms were removed before entering the model. Random intercepts for each participant were used as a random effect. Significant interactions were followed up by nested models to reveal detailed behavioral patterns. These analyses were conducted in R using lme4 package [56, 57].

Electrophysiological (EEG) data processing

EEG recording. Participants were comfortably seated in a sound attenuated room during the continuous electroencephalography (EEG) recording. Continuous EEG signals were recorded using the eego mylab system (ANT Neuro, Netherlands) and 64 channel waveguard caps during the Door task. Electrodes were mounted to the 10–20 international system with CPz as the on-line reference electrode, and AFz as the ground. The signals were amplified and digitized at a 1000 Hz sampling rate. Impedance of each electrode was maintained below 10 kΩ during recording.

Preprocessing. EEG preprocessing was performed in Matlab-based (Version: R2016b) EEGLAB (Version: 14.1.1b) and ERPLAB (Version: 7.0) toolboxes. Raw EEG data were first filtered using a band-pass filter between 0.1 and 40 Hz and a notch filter at 50 Hz, and re-referenced to whole-brain average. Ocular artifacts were corrected by Independent Component Analysis based on the Infomax (runica) algorithm. Continuous EEG data were then segmented into –200–800 ms epochs relative to feedback onsets, and baseline corrected using the average amplitude of –200–0 ms. Automatic artifact detection was performed using ERPLAB for all the EEG epochs across all channels to examine (1) peak-to-peak amplitudes higher than 150 μV within a 200-ms moving window with steps of 50 ms using the peak-to-peak function; (2) maximally allowed absolute amplitude (threshold: ±100 μV) throughout the whole epoch. All the EEG epochs were then visually inspected to ensure the quality before subsequent analysis. On average, 27.46 ± 2.55 feedback-locked epochs were included for each condition in the ERP analysis for each participant.

Event-related potentials (ERP). To analyze the RewP component, we averaged event-related potentials based on three Cue conditions (Gain, Control, and Loss cues) and two types of feedback (reward vs. non-reward). Secondly, based on the previous research [27], RewP was quantified as the mean amplitude of the 200–300 ms segments of reward minus non-reward difference wave, within the three Cue conditions separately, at electrode FCz. RewP from three conditions across two groups are presented in Figure 2.

Statistical analysis. Two Mixed Repeated-Measures Analyses of Covariance (ANCOVA) were used to compare the RewP amplitude and latency between conditions (within-subject: Gain, Control, and Loss) and groups (between-subject: Insomnia and Healthy), with age as a covariate. Age, as a proxy of maturity level, was controlled as a covariate as the sample covered a wide developmental span. Pearson correlation analysis was used to examine the associations between RewP amplitudes/latencies and the sleep/mood measures across all the participants. A sensitivity analysis revealed that, with our current sample size (28 vs. 29) and a power of 0.8, we could detect a Group difference with an effect size $d = 0.76$, and a within-subject difference of an effect size $d = 0.38$. Statistical significance was set at $p < 0.05$ and all the statistical analyses were conducted in Jamovi [58].

Results

Descriptive data

A hundred and six potential participants registered and expressed their interested in taking part in this study. Sixty-seven participants aged 15–25 completed the screening; five were excluded ($N = 1$ not meeting insomnia diagnosis, $N = 1$ with delayed sleep phase syndrome, $N = 2$ with major depression, $N = 1$ with obsessive compulsory disorder); and five dropped out before the completion of the study. All the

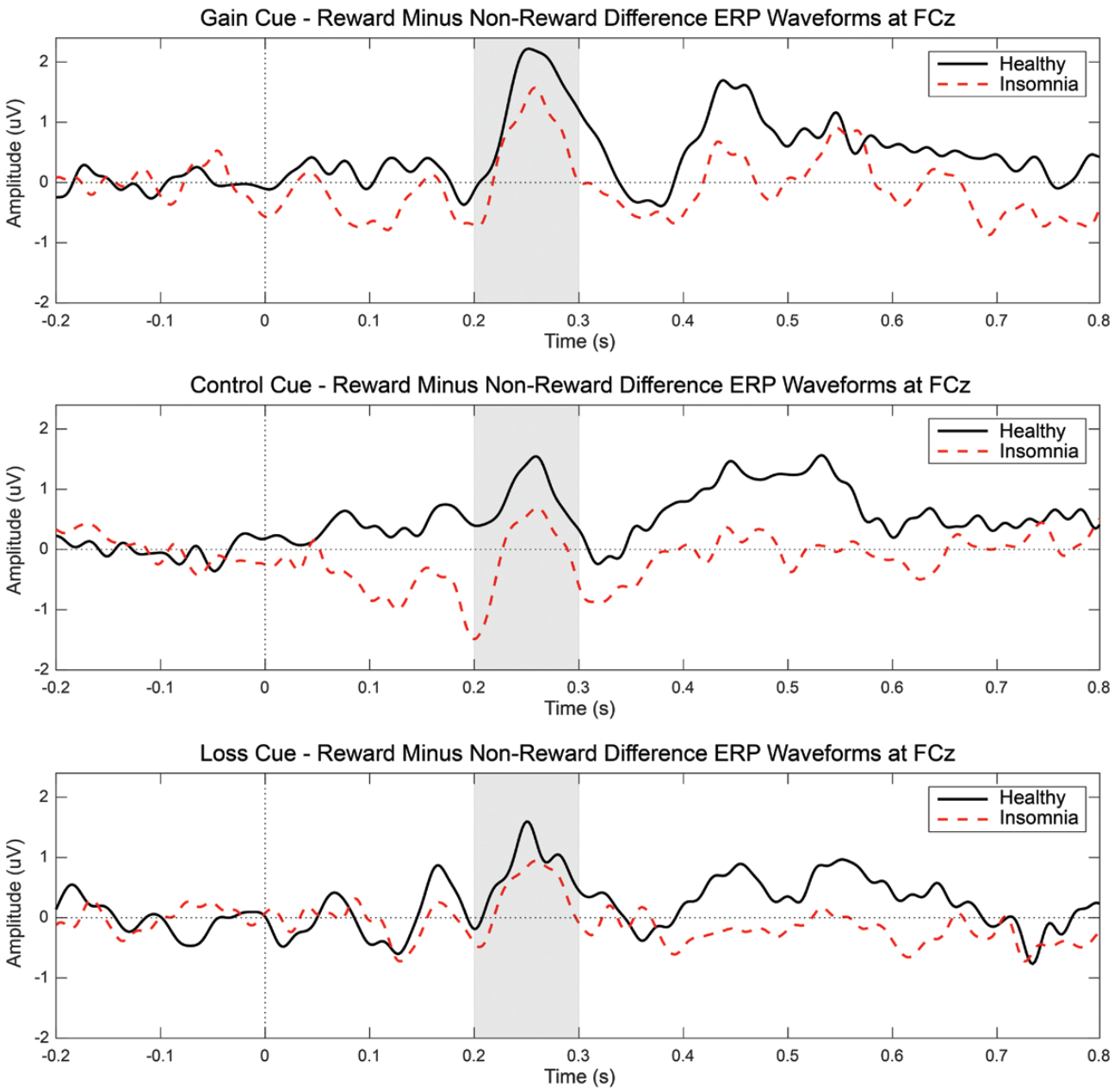

Figure 2. Group comparisons of RewP in three conditions. The averaged ERPs at electrode FCz of the reward minus non-reward difference wave were presented here for the three Cue conditions (Gain, Control, and Loss cues) separately.

participants were students from local secondary schools or universities. Twenty-eight participants (15 females, 2 aged below 18) in the insomnia group and 29 participants (17 females, 2 aged below 18) in the healthy sleeper group were recruited and completed the EEG experiment. There were no significant differences in age, gender, and chronotype preference between the two groups (see Table 1). Compared with healthy sleepers, participants in the insomnia group had significantly more subjective sleep disturbances as assessed by PSQI ($p < 0.001$), more severe insomnia symptoms as assessed by ISI ($p < 0.001$), lower sleep efficiency ($p < 0.05$), longer sleep onset latency ($p < 0.05$), longer wake after sleep onset ($p < 0.05$) and marginally longer time in bed ($p = 0.074$) as assessed by actigraphy. Insomnia group also had more mood disturbances (HADS-D, $p < 0.01$; and HADS-A, $p < 0.001$) and a higher level of suicidal ideation as assessed by DSI-SS ($p < 0.05$) than healthy sleeper group. Collapsing participants across insomnia and control groups, Supplemental Table 1 shows the correlations between the amplitudes and latencies of RewP and various measures assessing sleep and mood.

Behavioral performance

Regarding the estimation of the reward probabilities following three types of doors, there was no significant difference between insomnia group and healthy sleeper group (see Supplemental Table 2). Regarding trial-by-trial analyses of choices and RTs, we found a significant 3-way interaction (previous response × cue

Table 1. Comparisons of demographics, sleep measures, and mood disturbances between groups

	Insomnia group	Healthy sleeper group	t	p
	N = 28	N = 29	(χ^2 for gender)	
Demographics				
Female, *N* (%)	15 (53.6)	17 (58.6)	0.15	0.701
Age, *M* (*SD*)	20.64 (2.25)	21.00 (2.36)	–0.58	0.561
Self-report sleep measures, *M* (*SD*)				
PSQI	8.07 (2.24)	3.79 (1.59)	8.33	$p < .001^{***}$
ISI	14.14 (3.7)	3.79 (2.77)	11.99	$p < .001^{***}$
rMEQ	12.43 (3.32)	13.17 (3.41)	-0.83	0.408
Actigraphic measures, *M* (*SD*)				
TIB, min	489.36 (44.48)	469.06 (39.63)	1.82	0.074^
TST, min	431.66 (49.13)	436.45 (46.22)	–0.38	0.706
SOL, min	11.42 (8.83)	6.80 (6.10)	2.30	0.025*
SE, %	82.53 (4.80)	86.07 (4.14)	-2.98	0.004**
WASO, min	66.72 (20.88)	52.04 (19.74)	2.73	0.009**
Sleep diary, *M* (*SD*)				
TIB, min	509.95 (37.94)	495.98 (64.88)	0.92	0.365
TST, min	443.80 (40.87)	439.14 (40.81)	0.41	0.685
SOL, min	36.85 (19.01)	14.71 (9.90)	5.42	$p < .001^{***}$
SE, %	90.00 (5.70)	90.10 (6.50)	0.04	0.972
WASO, min	9.46 (7.45)	3.53 (5.95)	3.13	0.003**
Mood disturbances, M (SD)				
HADS-D	6.79 (6.64)	2.83 (2.61)	2.98	0.004**
HADS-A	8.29 (3.80)	4.72 (3.01)	3.93	$p < .001^{***}$
DSI-SS	0.36 (0.91)	0 (0)	2.11	0.039*

Note. ^ $p < 0.1$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
PSQI: Pittsburgh Sleep Quality Index; ISI: Insomnia Severity Index; rMEQ: Reduced Morningness-Eveningness Questionnaire; TIB: time in bed; TST: Total sleep time; SOL: sleep onset latency; SE: sleep efficiency; WASO: wake after sleep onset; HADS: Hospital Anxiety and Depression Scale (HADS-D: depression subscale, HADS-A: anxiety subscale); DSI-SS: Depressive Symptom Inventory-Suicidality Subscale.

type × group, $p < 0.040$) in predicting the current trial choices (see Supplemental Table 3). On average, 160.32 trials (*SD* = 19.41) per participant with valid RTs were included in the model. When examining nested linear mixed models in each group, we found that whilst insomnia participants tended to maintain their choices regardless of the cue type, healthy sleepers showed more strategic behavioral patterns: they were more likely to switch their choices (e.g. from left to right and vice versa) when they confronted with loss cues; but tended to maintain the same choice when they confronted with gain cues (see Figure 3, A and Supplemental Table 4). The absence of gain/loss framing-dependent trial-by-trial behavioral adjustment suggested that insomnia participants were insensitive to reward cues and were less efficient in adjusting their behavior given different types of reward cues.

Consistent results were found when we used cue type and group interaction to predict RTs (see Figure 3, B). In this model, average trial number with valid RTs was 161.30 (*SD* = 19.37) per participant. The significant two-way interaction ($p < 0.028$) was followed up by a nested model (see Supplemental Tables 5 and 6). We found that healthy sleepers became slower when they received loss cues ($p = 0.027$) and gain cues ($p < 0.001$) than control cues. In contrast, insomnia participants' RTs did not differ between gain and control cues ($p = 0.488$), whilst they were slower when they received loss cues ($p = 0.007$). Thus, RTs findings were consistent with the behavioral adjustment analyses that, whilst healthy sleeper participants were actively monitoring and adjusting their responses (both choices and RTs) based on different types of reward cues, insomnia participants did not show dynamic behavioral change patterns in response to these reward cues.

ERP results

To ensure the RewP scores were reliable, we examined the reliability of the FRN (Feedback-Related Negativity), that is, the ERP component on the same time window (200–300 ms) of each condition before the reward-minus-nonreward subtraction. FRN's reliability as a function of the number of trials was calculated via the ERP Reliability Analysis (ERA) Toolbox v 0.5.3 [59], which is based on the generalizability theory. We set a reliability threshold of 0.70 [60]. At the threshold of 0.70, the number of trials needed and overall dependability estimates for each condition, and the number of participants survived all the trial cutoffs in each group are reported in Supplemental Table 7. Specifically, 1 out of 28 participants was excluded in Insomnia group, 2 out 29 participants were excluded in Healthy Sleeper group. Thus, for the RewP measure, the valid participant number was 27 in Insomnia group and 27 in Healthy Sleeper group.

After excluding these three participants, the RewP of two groups in three cue types were plotted in Figure 2 (for the reward and nonreward ERP waveforms of each condition please see Supplemental Figure 1). We conducted two ANCOVA models on RewP amplitudes and latencies respectively, with Cue type (Gain, Control, and Loss) as within-subject variable and Group (Insomnia and Healthy Sleeper) as between-subject variable, whilst controlling for age (Table 2). As shown in Figure 2 and

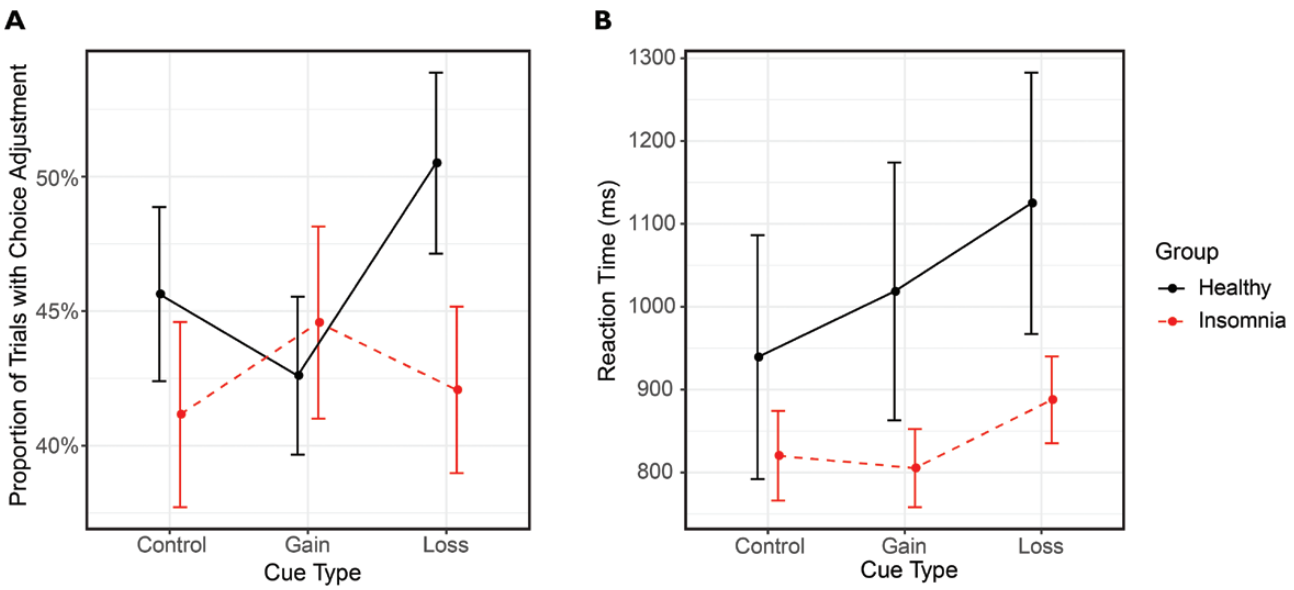

Figure 3. (A) Interaction between Cue type and condition on the proportion of trials with choice changes. Mean and standard error (error bar) were plotted. While healthy sleepers tended to change their choices upon Loss cues, insomnia participants maintained their choices across all three Cue types. Results reported in text were modeled on trial level. Here the proportion of trials with choice adjustment was first calculated on subject level, then averaged on group level for demonstration purpose. (B) Reaction time contrasts across three Cue types between two groups. Mean and Standard Error (error bar) were plotted. Healthy sleepers took time on their decisions upon Gain and Loss cues, while insomnia participants lacked such prudence even when the consequence was reward related. Results reported in text were modeled on trial level. Here reaction time was first calculated on subject level, then averaged on group level for demonstration purpose.

Table 2. RewP amplitudes and latencies

	Insomnia group	Healthy sleeper group	*F*-Interaction	*F*-Group	*F*-Cue
	Mean (*SD*)	Mean (*SD*)			
Gain amplitude (μV)	0.676 (1.592)	1.390 (1.741)	0.34	4.95*	0.87
Control amplitude (μV)	–0.013 (1.805)	0.887 (1.559)			
Loss amplitude (μV)	0.428 (1.692)	0.824 (1.773)			
Gain latency (ms)	250.963 (22.650)	254.889 (20.444)	1.41	0.94	0.69
Control latency (ms)	260.667 (19.287)	252.222 (21.918)			
Loss latency (ms)	260.444 (22.900)	253.778 (22.541)			

Note. * $p < 0.05$.

Table 2, the model of RewP amplitude revealed a significant main effect of Group, F (1, 51) = 4.95, p = 0.031, η_p^2 = 0.088, with reduced RewP amplitudes among insomnia patients compared to healthy sleepers, $t(51) = -2.23$, $p_{Bonferroni}$ = 0.031. The main effect of Cue type was not significant, $F(2, 102) = 0.87$, p = 0.424, η_p^2 = 0.017; nor was the interaction between Cue type and Group, $F(2, 102) = 0.34$, p = 0.711, η_p^2 = 0.007. Age did not have a significant main effect as a covariate, $F(1, 51) = 1.55$, p = 0.219, η_p^2 = 0.030, and there was no interaction between age and Cue type, $F(2, 102) = 0.62$, p = 0.541, η_p^2 = 0.012. Regarding RewP latencies, there were no significant effects of Cue type, $F(2, 102) = 0.69$, p = 0.502, η_p^2 = 0.013; Group, $F(1, 51) = 0.94$, p = 0.338, η_p^2 = 0.018; and interaction: $F(2, 102) = 1.41$, p = 0.250, η_p^2 = 0.027. There was no significant main effect of age as a covariate, $F(1, 51) = 0.07$, p = 0.796, η_p^2 = 0.001, and there was no significant interaction between age and Cue type, F (2, 102) = 0.63, p = 0.537, η_p^2 = 0.012.

Discussion

This study investigated the association of insomnia with reward processing independent of mood disorders in youth. As hypothesized, non-depressed youths with insomnia disorder showed an absence of active behavioral adjustment and more blunted reward positivity during the Cued Door task than their healthy sleeper counterparts, indicating disrupted neural response to reward. Our results demonstrated the neural underpinning of altered reward responsiveness in relation to sleep problems such as insomnia.

The present study provided direct evidence that insomnia disorder was associated with the disruption of reward processing in adolescents and young adults. Several lines of research has suggested a link between sleep disruption and altered reward processing. For example, a genome-wide association study found that the insomnia-related genetic variants (i.e. 202 significant risk loci) were associated with neurons implicated in reward processing (i.e., striatal medium spiny neurons and hypothalamic neurons) [61]. In addition to the genetic basis, there is also a neurobiological basis for the association between sleep and reward functioning, potentially mediated by the reduced recruitment of the caudate in adults with insomnia [62] and healthy adolescents with sleep disruption [36]. The findings of our study lend further support for the association between

insomnia, a clinical sleep disorder, and reward dysfunctions, by demonstrating more blunted reward positivity amplitudes in youths with insomnia.

Given the consistent evidence, it is important to understand the psychological implications of reward insensitivity in insomnia. In this study, the trial-by-trial analysis revealed a lack of flexible behavioral adjustment during the reward decision-makings in the insomnia group. Our results were in line with a previous study that found lower reward dependence temperament in insomnia patients as compared with healthy sleepers [63], suggesting that reward insensitivity could be a stable trait in insomnia. In other words, abnormal reward processing might be underlying the cognitive and socio-emotional dysfunctions in insomnia, in that the lack of reward-dependent flexibility might interfere with one's ability in problem solving, goal-directed behavioral adjustment [64] and regulating emotions [65, 66] in a dynamic environment. Note that acute sleep deprivation also led to impaired decision making characterized by a lack of flexibility [67–69], which was in compliance with the findings of this study. Sleep disruption has also been found to be associated with impaired emotional regulation [65, 66], and lower empathic sensitivity to negative stimuli, suggestive of a reduced ability to feel empathy towards the emotions experienced by others [70]. In patients with insomnia, functional and/or structural abnormalities have been observed in orbitofrontal cortex [71], prefrontal cortex [72–75] and amygdala [76, 77], which are the brain areas responsible for the processing of emotional and social information [78–83]. Therefore, blunted reward processing might also explain the experience of emotions in insomnia, as reward and emotion are interrelated processes associated with amygdala [78, 84]. For example, patients with insomnia were found to give reduced ratings of emotion intensity for sad and fearful facial expressions [85], and be less accurate in identifying angry faces than healthy sleeper controls [86]. Future studies are needed to better understand the impacts of reward insensitivity on the experience of insomnia, especially in terms of socio-emotional functioning.

In the current study, we found that insomnia per se was associated with reduced reward processing as evidenced by blunted reward positivity, which has been proposed as a biomarker of depression [27]. The reward positivity has been found to be associated with higher distress-based symptoms including worry, rumination, and depressed mood [87]. In addition, cognitive behavioral therapy for depression has been shown to result in positive changes in reward processing among adolescents [88]. Moreover, reward processing has been found to closely interact with sleep disruption in predicting later development of depression in adolescents [34, 35], supporting the role of reward processing in explaining the high comorbidity of depression in insomnia. However, it remained unclear what role reward processing would play in the course of insomnia disorder, especially in relation to the trajectory of the development of depression. A previous study also found that insomnia patients with low reward dependence responded worse to the psychological treatment for insomnia [63], highlighting the need for increased clinical attention to improving reward sensitivity in devising treatment for insomnia. Based on our data, clinicians might consider including treatment strategies with a focus on improving reward functioning in individuals with insomnia disorder, via (1) explicit behavioral adjustment training in a reward task with a focus on improving one's behavioral adjustment to response to reward cues; and (2) explicit reward sensitivity training with a focus on inducing higher internal reward dependence.

This study provided the evidence on the neurophysiological basis of altered reward processing in non-depressed youth insomnia patients. However, some limitations should be noted. First, the cross-sectional nature of this study prohibited the inferences about the casual relationship between insomnia and reward deficits. There is a need for longitudinal studies to further delineate the prognostic implications of altered neural response to reward in insomnia in relation to the development of psychopathology. In addition, whilst the participants in the present study were diagnosed with insomnia disorder as confirmed by clinical interview, there was a lack of polysomnography (PSG) to rule out other comorbid sleep disorders and provide polysomnography-based objective sleep parameters. Future studies could consider recording overnight EEGs to establish direct links between sleep-related physiological activities and wakeful reward dysfunction as well as impaired behavioral adjustment shown in this study.

Conclusions

In this study we found that insomnia disorder was associated with a more blunted reward positivity indicating disrupted reward processing, independent of mood disorders. In addition, reward-processing alteration might also be underlying the etiology and pathogenesis of insomnia. Future longitudinal studies are needed to better understand the long-term effects of insomnia-related reward dysfunctions on the risk of developing mood disorders.

Supplementary material

Supplementary material is available at *SLEEP* online.

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