Version No: 4
Date: 29 May 2025

Research Protocol

An Exploratory Study of the Relationship between Substance Use, Sleep Disturbances and Reward Sensitivity – A Randomized Control Trial of Cognitive Behavioral Therapy for Insomnia

Yeung Wing Chun, Fritz

Clinical Psychologist

Kwai Chung Hospital

Table of Contents

Abstract

Disruption in reward sensitivity was known as a key factor in the development and maintenance of Substance Use Disorder (SUD). Past research found blunted responses to neutral stimuli and heightened responses to substances in patients with substance misuse. Meanwhile, sleep disturbances often presented in patients with substance misuse and were found to alter brain reward circuitry. The objective of the present study investigates the effect of brief Cognitive Behavioral Therapy for Insomnia in individuals with substance use. Changes in sleep parameters, substance use, and measurements of reward sensitivity are compared between treatment group and active control group. The findings of this study will contribute to a better understanding of the underlying mechanism of substance use and inform treatment formulation.

Introduction

Substance misuse is a significant social and mental health concern in Hong Kong, as it incurs substantial expenses to the public health system (Liu, 2019). In a recent local study, a trend of increasing number of elderly substance abusers and increasing severity of drug abuse in middle-aged and younger adolescent groups was found (Liu, 2019). Nonetheless, substance use disorder is often considered a difficult condition to treat. First, co-occurrence of other psychiatric symptoms was common in people with substance use, possibly because of shared vulnerabilities between substance use and psychiatric disorders (Koob, 1992). The "dual diagnosis" complicated the clinical picture, making it difficult for clinicians to decide treatment focus. Individuals with substance misuse were also found to have high rates of relapse using traditional treatment approaches that focused on reduction of substance use (Koob & Volkow, 2016). For example, previous research found that 40% to 60% of individuals with substance use disorder had relapse for substance use within 1 year after seeking treatment (Bowen et al., 2014). It was explained that the underlying needs of the individuals, e.g., mood problems, sleep disturbances, and family problems, were not adequately addressed by traditional relapse prevention approaches that mainly focused on increasing avoidance-based goals to reduce triggering substance use (Bowen et al., 2014). Another difficulty was that individuals with substance misuse tended to show limited willingness to receive traditional treatment for quitting substance use. Individuals with substance misuse could see limited values to receive treatment for managing substance use (McHugh et al., 2010). They might be in denial of the severity of consequences associated with substance use (McHugh et al., 2010). Stigma associated with substance use also could maintain their sense of shame and reluctance to disclose substance use (Kelly et al., 2017). In view of these difficulties, it was suggested that effective treatment approaches for substance

misuse should consist of a number of active treatment components to maintain individuals' motivation to engage in treatment (McHugh et al., 2010).

Sleep Disturbances and Substance Misuse

Sleep disturbances were often reported as co-occurring symptoms in the substance use population across different types of users. In a sample of 123 treatment seeking patients with alcohol use disorder, 45% of participants reported moderate level of insomnia symptoms in Insomnia Severity Index, and 29% reported their symptoms to be mild (Chaudhary, 2015). In another sample of 303 treatment seeking samples, 88% of patients with alcohol use disorder reported insomnia during the early recovery stage (Kolla et al., 2020). Over 75% of cannabis users in recovery reported sleep disturbances and used tranquilizers, alcohol, or relapsing to cannabis to improve sleep quality (Copersino et al., 2006). Stein et al. (2004) found that 85% of patients with opioid use disorder who received methadone maintenance rated a score of 6 or higher on the Pittsburgh Sleep Quality Index (PSQI), indicating a significant level of sleep disturbances. Eight-four percent of patients who were admitted to hospital for detoxification of benzodiazepine, alcohol, heroin, cocaine, and cannabis reported to have insomnia symptoms during active substance use (Grau-López et al.,2016). Chakravorty and colleagues (2018) opined that the direct effect of substance use on sleep, withdrawal syndromes of substance use, and co-occurring psychiatric conditions were all the possible contributing factors of sleep disturbances.

Furthermore, it was found that sleep disturbances experienced in adolescence predicted substance use later in the individuals' life. Adolescents who self-reported to experience symptoms of insomnia were more likely to report use of alcohol, cannabis, and drugs other than cannabis in adulthood (Roane & Taylor, 2008). In another longitudinal study, consistency of sleep pattern and sleep duration predicted the onset of substance use two years later among teenagers (Pasch et al., 2012). Hasler and colleagues (2014) also found

that teenagers who reported more variation in sleep times at baseline reported more symptoms of alcohol use disorder at 3- and 5-year follow-up.

Conroy and Arnedt (2014) proposed that the relationship between substance use and sleep disturbances might be bi-directional. Rosenblum (2017) suggested that individuals with sleep problems could be more prone to self-medication with substances, while substance use might further interfere with sleep. In an experience sampling study, the temporal relationship between craving for substance use and sleep difficulties was studied (Freeman & Gottfredson, 2018). It was found that worse sleep predicted a higher level of drug cravings, while stronger cravings also significantly predicted worsened sleep outcomes. It was hypothesized that sleep loss and circadian misalignment could disrupt reward-related brain function and in turn, contribute to substance use (Hasler et al., 2014).

Reward Sensitivity in Individuals with Sleep Disturbances and Substance Misuse

In earlier years, researchers conceptualized that individuals' responsiveness to rewarding stimuli were governed by the Behavioral Activation System (BAS; Gray, 1987). Individuals with a more reactive BAS were believed to be more motivated to approach and engage with pleasurable stimuli, and they experience stronger positive emotions in response to rewards (Carver & White, 1994). These individuals were believed to have higher reward sensitivity. In recent years, researchers have adopted brain imaging to investigate the brain's response to pleasurable stimuli (Volkow et al., 2010). Ventromedial prefrontal cortex and ventral striatum were considered a key brain region responsible for reward processing (Pujara et al., 2016). It was found that sleep disturbances altered brain reward circuitry (Motomura et al., 2017). In patients with chronic insomnia, they showed reduced activation in ventral striatum in response to natural cues such as food or money (Motomura et al., 2021). Youth with insomnia disorder was found to have blunted reward sensitivity and inflexibility in decision-making in an experimental monetary paradigm (Ling et al., 2022). Mullini et al.

(2013) found that temporary sleep deprivation produced aberrant functioning in the neural reward circuit.

Dysfunction in reward circuitry was also found in individuals with substance misuse. Dugré, Orban, and Potvin (2023) reviewed 96 studies, which investigated brain imaging of 5757 subjects in total, and found highly consistent findings of hyper-connectivity of ventromedial prefrontal cortex and ventral striatum in individuals of different substance misuse across research studies. Heightened reward sensitivity to substances was supported by the assessment of dopamine neurocircuitry (Volkow & Blanco, 2023). Individuals with substance use disorder showed consistent reduction in striatal D2 receptors which led to increased sensitivity towards substance use (Volkow & Blanco, 2023). Researchers also found that individuals with substance dependence showed poorer performance in the Iowa Gambling Task (Fridberg et al., 2010; Grant et al., 2000). These individuals were found to favor choices that brought about small, immediate gains but larger losses over time in the Iowa Gambling Task, which supported the presence of dysfunction in reward sensitivity (Fridberg et al., 2010; Grant et al., 2000). In a sample of participants with comorbid bipolar disorder and stimulant use disorder, the poorer performance in the Iowa Gambling Task predicted heavier use in stimulants at a future time point (Nejtek et al., 2013).

Some researchers focused on studying the reward deficiency hypothesis in individuals with substance use (Bowirrat & Oscar-Berman, 2005), in reference to a reduction in sensitivity towards natural stimuli, such as food or social cues. The reduction in sensitivity to natural stimuli was believed to contribute to a higher relative-reinforcing value of the hedonic effects of drug consumption. Clinical brain-imaging studies supported the hypothesis, as a decrease in activation of brain regions implicated in the processing of food, sexual, or monetary rewards was found in individuals with addiction (Volkow & Blanco, 2023).

Considering these findings, alternation in reward sensitivity likely played a crucial role in the relationship between sleep disturbances and substance misuse (Conroy & Arnedt, 2014).

Brief Behavioral Treatment for Insomnia in People with Substance Misuse

As sleep problems were found to affect reward sensitivity and substance misuse, researchers also started investigating the effect of psychological treatment on insomnia among individuals with substance misuse. Guo et al. (2023) opined that use of different substances all resulted in changes in sleep and improving sleep quality should serve as a complementary treatment target for patients with substance misuse. Furthermore, psychological interventions were considered a safer alternative in treating sleep problems to pharmacological interventions (Speed et al., 2022). Targeting symptoms of insomnia in psychological treatment was also considered a less stigmatizing focus compared to conventional substance misuse treatment (Hasler et al., 2014), and would likely benefit initial patient engagement.

Cognitive Behavioral Therapy for Insomnia (CBTi) was set to address the underlying causes of insomnia and improve sleep quality (Perlis et al., 2005). It covered several core cognitive and behavioral techniques including stimulus control, sleep restriction, and cognitive restructuring. There has been strong evidence supporting the effect of CBTi in reducing symptoms of sleep disturbances. In a meta-analysis, CBTi was found to be as effective as pharmacological interventions for patients with primary insomnia and its effect was more lasting (Mitchell et al., 2012). Specifically targeting the substance misuse population, several studies reported substantial effects of CBTi. For example, Mijnster et al. (2022) reviewed the effectiveness of CBTi for individuals with alcohol use and hypnotic dependence and found a general trend of reduction in insomnia symptoms as measured by Insomnia Severity Index. Arnedt et al. (2011) found a significantly larger reduction of insomnia severity in recovering individuals with alcohol use who received CBTi compared to

those receiving placebo interventions. In cannabis users, Arnedt et al. (2023) found a significantly larger reduction of insomnia severity in those who received CBTi compared with those who received sleep hygiene education only. Miller et al. (2023) found that CBTi produces statistically significant reductions of large effect sizes in insomnia severity and substance use among adults seeking treatment for substance use, although the study did not have a control group to account for potential confounds. Among cannabis users in the study of Arnedt et al. (2023), more significant reduction in cannabis use at the 8th week post-treatment follow-up was found in participants who received telephone-based CBTi than in the active control group who received sleep hygiene education. Overall, CBTi appeared to be effective in reducing both insomnia symptoms and substance use among individuals with substance misuse. Nonetheless, maintaining participation in standard CBTi of 6 to 8 weeks might be challenging. Among a sample of 528 patients attending sleep clinic, it was found that 40% of participants did not complete all 7 in-person sessions of CBTi (Ong, Kuo & Manber, 2009). In an 8-week CBTi study focusing on patients with alcohol dependence, the dropout rate of intervention group exceeded 30% (Arnedt et al., 2011).

Researchers developed brief versions of CBTi while maintaining its effectiveness. Ellis, Cushing, and Germain (2015) found that a single-session CBTi produced significant improvements in Insomnia Severity Index scores among patients with sleep problems, and reported medium to large effect size when comparing intervention group to a control group. Bishop et al. (2021) conducted session-by-session analysis and found that majority of the treatment effect on sleep disturbances occurred over the first two sessions of CBTi that focused on stimulus control and sleep restriction. Another treatment protocol, the Brief Behavioral Treatment for Insomnia (BBTI) reduced the number of in-person visits to 2 sessions, and focused on the early implementation of stimulus control and sleep restriction principles, similar to the approach used in CBT-I (Gunn, Tutek & Buysse, 2019). However,

unlike CBT-I, BBTI did not target inaccurate beliefs and attitudes regarding sleep, insomnia, or the effects of poor sleep. A meta-analysis reported that Brief Behavioral Treatment for Insomnia (BBTI) leads to significant improvements in insomnia, as measured by subjective sleep assessments and the benefits were particularly obvious within 1 to 2 months of implementation (Kwon et al., 2022). BBTI was also initially used in the substance use population. In a pilot study focusing on individuals exposed to trauma, BBTI showed large effect sizes in reducing insomnia symptoms and cannabis use when comparing to waitlist control group at 3-month follow up (Short, Zvolensky & Schmidt, 2021).

Summary

In summary, research literature suggested that there is a high prevalence of sleep disturbances among individuals with substance misuse. Both substance use and sleep problems are believed to affect reward sensitivity, while reward sensitivity is considered a key factor in maintaining substance use. Recent research has shown that brief CBTi effectively reduces the severity of insomnia in patients with substance use. Several studies also found a positive impact of brief CBTi on reducing substance use. Nonetheless, the hypothesis that sleep problems disrupt reward-related brain function and contribute to substance use has not been adequately tested.

Therefore, the purpose of the proposed study is among the first attempts to examine the relationships among substance use, sleep disturbances, and reward sensitivity. It also aims to investigate whether reward sensitivity plays a role in the mechanism by which sleep interventions help reduce substance misuse. Although focusing on managing sleep problems is considered a less stigmatizing and safer treatment for managing sleep problems among individuals with substance misuse (Hasler et al., 2014), it is important to highlight that the effect and mechanism of sleep interventions on individuals with substance use problems have not been studied in the Hong Kong community. This study will provide evidence on the

significance of sleep interventions in treating substance misuse, addressing patient needs more effectively and improve treatment engagement.

Hypotheses

The present study is separated into two phases to test four hypotheses on the associations among sleep disturbances, reward sensitivity, and substance use.

Hypothesis 1: Brief CBTi group shows a larger improvement in sleep quality, reduction in insomnia symptoms, and reduction in symptoms of substance use than active control group (i.e., sleep education group).

Hypothesis 2: Changes in reward sensitivity from baseline to post-treatment mediate the effect of intervention group assignment (i.e., brief CBTi or Active Control) on changes in substance use from baseline to post-treatment and those from baseline to one-month follow-up.

Methodology

Participants

Based on power analysis, a total of 154 participants will be recruited. All participants will be recruited from Substance Abuse Assessment Clinic and other psychiatric out-patient clinics of Kwai Chung Hospital. Individuals with problematic substance or alcohol use in the past 3 months and sleep disturbances will be recruited. Specifically, the Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS) and Insomnia Severity Index (ISI) tools will be used to screen participants for eligibility. Scores higher than or equal to 1 in both TAPS-1 and TAPS-2 indicates problematic substance use in the past 3 months and a score higher than or equal to 8 on the ISI indicates presence of subclinical insomnia symptoms. Participants who meet these criteria will be considered for inclusion in the study. Participants will be randomly assigned, in an open-label format and at a 1:1 ratio, to receive either brief Cognitive Behavioral Therapy for Insomnia (CBTi), or Sleep Education (SE).

There are several exclusion criteria. Individuals who cannot understand Cantonese, cannot read Traditional Chinese, or cannot provide informed consent due to, for example, intoxication or abnormal mental state will not be recruited. Individuals will also be excluded from the studies if they report abnormal or unstable mental states, such as active psychotic symptoms or acute intoxication, at any point of the study. Individuals who work overnight or have rotating shifts and individuals who report regular use of hypnotics, pregnancy or medical conditions (e.g. sleep apnea) that may have a severe impact on sleep will be excluded from this study as well.

At any stage of the study, if immediate intervention needs (e.g. suicidal risk) are identified, the individuals will be contacted as soon as feasible. Immediate intervention needs may be indicated by participants' responses to Question 27 and 28 of the General Health Questionnaire, "You found yourself wishing you were dead and away from it all?" and "You found that the idea of taking your own life kept coming into your mind?", or clinical observations or self-reported signs of unstable mental state, such as severe withdrawal symptoms or psychotic symptoms. The participant will be contacted for further assessment by Clinical Psychologist, and referred to appropriate services if needed, within one working day.

Measures

The Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS; McNeely et al., 2016)

The Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS) Tool includes an initial screening section (TAPS-1) and a subsequent brief assessment (TAPS-2) for individuals who receive a positive screening result. This tool aims to identify problematic substance use over the prior three months. For screening illicit and prescription

drug misuse using a cut-off score of 1, sensitivity varied between 63% and 82%, while specificity exceeded 93% (McNeely et al., 2016).

General Health Questionnaire (GHQ-28; Goldberg & Hillier, 1979)

GHQ-28 is a self-report questionnaire to screen for potential psychological disorders in terms of difficulties in performing everyday activities and presences of distressing symptoms (Goldberg & Hillier, 1979). Test-retest reliability of GHQ-28 is high, ranging from 0.78 to 0.90 (Robinson and Price, 1982), and it shows good correlation with other mood measurement tools (Robinson and Price, 1982; Sakakibara et al., 2009).

Insomnia Severity Index (ISI; Bastien, Vallières, & Morin, 2001)

ISI is a well-validated self-report questionnaire specifically designed to assess the severity of insomnia symptoms. It measures the perceived severity of insomnia-related difficulties, including difficulties falling asleep, staying asleep, and early morning awakenings, as well as the impact of insomnia on daytime functioning. Insomnia Severity Index (ISI) shows acceptable internal consistency (Cronbach's alpha = 0.74) and satisfactory convergent validity, as the individual items on the ISI correlate reasonably well (r = 0.32 to 0.91) with indicators on a sleep diary (Bastien, Vallières & Morin ,2001).

Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989)

PSQI assesses overall sleep quality over a one-month period. In addition to sleep disturbances measured by ISI, it covers measurements on the quality of sleep, including sleep duration, latency, disturbances, medications, and daytime dysfunction for a comprehensive understanding of an individual's sleep functioning. The test-retest reliability of PSQI is high (r = 0.87; Backhaus et al., 2002). It has a sensitivity of 98.7% and a specificity of 84.4% for assessing sleep disturbances in insomnia patients versus controls, when using a PSQI total score threshold of higher than 5 (Backhaus et al., 2002).

Drug Use Disorders Identification Test (DUDIT; Berman et al., 2005)

The Drug Use Disorders Identification Test (DUDIT) is a self-report questionnaire aiming to evaluate the intensity of their drug use. It targets both use of illegal drugs and non-medical use of prescription drugs. The DUDIT comprises 11 questions that address different aspects of drug use, including the frequency of use, symptoms of dependence, and negative outcomes linked to drug use. Based on the score on the DUDIT, the extent of drug-related problems will be determined, with higher scores indicating more severe drug use concerns. DUDIT shows satisfactory reliability and validity as a research tool (Hildebrand, 2015), with an internal consistency (Cronbach's α) of 0.90 or higher, adequate sensitivity (85% to 100%), and satisfactory specificity (75% to 92%).

Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993)

The Alcohol Use Disorders Identification Test (AUDIT) is a widely used tool for assessing the severity of alcohol use. It is a self-report questionnaire that consists of 10 items covering alcohol consumption, drinking behavior, and alcohol-related consequences. The AUDIT assesses the frequency and amount of alcohol consumed, signs of alcohol dependence, and negative outcomes stemming from alcohol use. Based on the score on the AUDIT, the extent of alcohol-related problems can be determined, with higher scores indicating more severe alcohol use concerns. AUDIT demonstrates high internal consistency (i.e., an average Cronbach's alpha of 0.80; de Meneses-Gaya et al., 2009). Additionally, its sensitivity and specificity generally exceed those of the other assessments of hazardous drinking (Reinert & Allen, 2007).

Sensitivity to Reward scales from Sensitivity to Reward and Sensitivity to Punishment Questionnaire (SRSPQ; Torrubia et al., 2001)

The Sensitivity to Reward Scales from SRSPQ consists of 24 items for assessing reward sensitivity and uses a dichotomous scale (“Yes” and “No”). Unlike other scales that measure reward sensitivity, items on the Sensitivity to Reward Scales assess specific rewards,

such as money, social rewards, sexual rewards and alcohol and substances. The use of specific concepts of rewards to measure reward sensitivity helps reduce ambiguity when interpreting results (Torrubia et al., 2001). The Sensitivity to Reward Scale demonstrates good internal consistency (Cronbach's alpha = .75-.78) and test-retest reliability (r = .61-.87; Torrubia et al., 2001).

Computerized Iowa Gambling Task (Bechara et al., 1994)

The Iowa Gambling Task was originally designed to identify decision-making deficits in patients with lesions in the ventromedial prefrontal cortex (vmPFC) versus other brain areas (Bechara et al., 1994). In the task, participants are instructed to gain as much as possible by choosing from one of four options. They are informed that each option will yield a gain and possibly a penalty. They are also informed that some decks are more advantageous than the others. However, they are not informed that there are 100 trials in total. Two of the choices are disadvantageous which provide immediate large rewards but more significant losses eventually. The remaining two decks are more advantageous, giving modest reward and lower losses.

Traditionally, the score of the Iowa Gambling Task is to index the net number of cards chosen from advantageous decks; however, this approach neglects the multiple decision-making process (Chan, 2014). To measure reward sensitivity of participants from their task performance appropriately, Prospect Valence Learning (PVL) model, a validated cognitive model of IGT (Ahn et al., 2008), will be applied. The PVL model suggests that participants make their card decision based on valence expectation, which is composed of motivational parameter and learning as well as response consistency (Ahn et al., 2008). Motivational parameter is further differentiated into feedback sensitivity and loss aversion (Ahn et al., 2008); in particular, feedback sensitivity refers to the non-linear relationship between the actual quantities of gain or loss and the prospect valence, and this construct

represents Reward Sensitivity of task performance in the present study. Previous study showed that the cognitive model of IGT identified significant differences in motivational parameters in individuals with substance use when compared with healthy controls (Fridberg et al., 2010).

Client Satisfaction Questionnaire (Larsen et al., 1979)

To better understand the participants' subjective experiences about treatment sessions, participants will be invited to rate their satisfaction using an 8-item Client Satisfaction Questionnaire (CSQ) developed by Larsen et al. (1979) at the last treatment session. The CSQ is designed to assess the satisfaction levels of patients with health and human service systems and shows an internal consistency of Cronbach's α = .93 (Attkisson & Zwick, 1982).

Interventions

Both treatment groups will receive 3 in-person treatment sessions in total. Participants will attend 3 in-person sessions at Week 1, Week 4 and Week 8, and two telephone follow-up at Week 2 and Week 3. For CBTi group, the content of the sessions will be adapted from Perlis et al. (2005) and Gunn, Tutek & Buysse (2019) and will focus on techniques such as stimulus control and sleep restriction (See Table 1). Individuals will also be prescribed with sleep diary in each session. Sleep diary will be reviewed at the beginning of each subsequent session. As an active control condition, Sleep Education sessions focuses on psychoeducation sessions on sleep hygiene (See Table 2).

Table 1

Outline of Brief Cognitive Behavioral Therapy for Insomnia Group

Session	Outline

Week 1 Sleep Scheduling & Cognitive Strategies (60 minutes)	Concepts of cognitive behavioral therapy will be introduced. Sleep restriction and stimulus control techniques will be introduced. Behavioral strategies focusing on increasing sleep drive will be discussed to improve sleep quality, duration, and timing. Concepts of maladaptive beliefs about sleep will be explained
Week 2 & 3 Telephone Boosters (<20 minutes each)	Sleep quality, diaries, daytime functioning will be reviewed to facilitate adherence to recommendations suggested at session 1. Further sleep titration will be conducted if indicated.
Week 4 Progress Review (30 minutes)	Sleep titration will be conducted by reviewing sleep diary and adjusting time in bed appropriately. Understanding of maladaptive beliefs about sleep will be further enhanced. Factors related to relapse of insomnia and strategies for adjusting sleep patterns will be discussed.
Week 8 Booster Session <20 minutes)	Sleep titration will be conducted by reviewing sleep diary and adjusting time in bed appropriately.

Table 2

Outline of Sleep Education Group

Session	Outline
Week 1 Introduction & Sleep Education (60 minutes)	Concepts of insomnia will be discussed. Sleep hygiene will be introduced.
Week 2 & 3 Telephone Boosters (<20 minutes each)	Key concepts from Session 1 will be discussed.
Week 4 Progress Review (30 minutes)	Concepts of insomnia and sleep hygiene will be reviewed.
Week 8 Final Booster Session (<20 minutes)	Overall summary and review of sleep hygiene.

Fidelity Check of Interventions

A checklist will be adapted from Taylor et al. (2019) for the evaluation of intervention fidelity. The checklist will consist of behavioral descriptions on the session content. A trained research assistant will sit in 20% of treatment sessions at random and rate the session contents accordingly.

Procedure

Participants will be recruited from Substance Abuse Assessment Units, and other psychiatric outpatients at Kwai Chung Hospital (KCH) and all research procedures will be carried out at the respective clinics at KCH. Recruitment poster will be displayed in these clinics. Participants will first complete the tools (TAPS & ISI) to screen for eligibility. Informed consent will be obtained from all participants before their enrolment in the study. Enrolled participants will be invited to further complete the self-report measures and gambling tasks (PSQI, AUDIT DUDIT, SRSPQ and Iowa Gambling Task) to assess sleep problems, substance use severity and reward sensitivity at baseline. GHQ-28 will also be administered to control for mood symptoms. Demographic data, including participant's age, gender, marital status, employment status, education level, and use of psychiatric medication will also be collected. CBTi participants will go through two in-person sessions of brief CBTi at Week 1 and Week 4. Booster telephone follow-ups will be made at Week 2 and Week 3. Active Control group will receive a sleep education session at Week 1, followed by 2 weekly follow-up booster calls while continuing their usual treatment. Post-intervention measurement will be conducted at Week 4 for both groups after receiving in-person intervention sessions. Both groups will be re-assessed at Week 8 before a final in-person booster session.

Treatment and data collection sessions will be conducted by Clinical Psychologists, trained Clinical Psychology trainees, or trained Psychology Assistants.

Planned Data Analysis

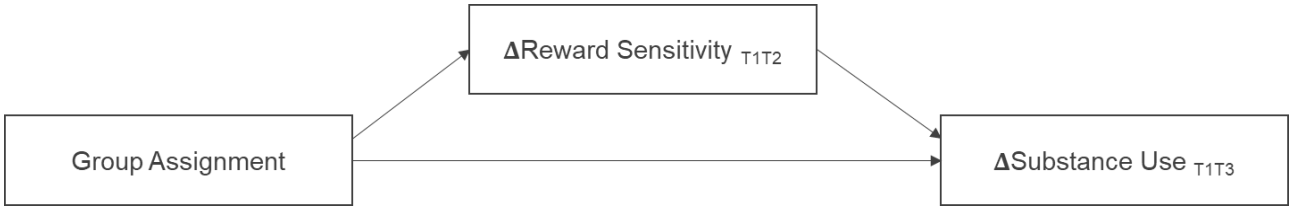
For Hypothesis 1, ANCOVA will be used. Intervention group ("Group") would be entered as an independent variable. Sleep duration ("SLDU_t1"), total scores of ISI ("ISI_t1"), PSQI ("PSQI_t1"), ("AUDIT_t1") and ("DUDIT_t1") at baseline will be entered as covariate. Sleep duration ("SLDU_t2, "SLDU_t3"), total scores of ISI ("ISI_t2",

"ISI_t3"), PSQI ("PSQI_t2", "PSQI _t3"), ("AUDIT_t2", "AUDIT_t3") and ("DUDIT_t2", "DUDIT_t3") at Week 4 and Week 8 will be entered as dependent variables. Effect sizes on treatment-induced changes will be computed as appropriate.

To explore the directionality of relationships among the variables in Hypothesis 2, cross-lagged mediation analysis will be performed using structural equation modelling. Standardized residualized change scores (SRCSs) will be computed for mediator (i.e., Reward Sensitivity) and outcome measures (i.e., Substance Use), with the effect of measurement at the prior time point (e.g., T2) partialled out of that for the current time point (e.g., T3). The SRCSs of Reward Sensitivity and Substance Use will be entered to a cross-lagged path model (see Figures 1 and 2).

Figure 1

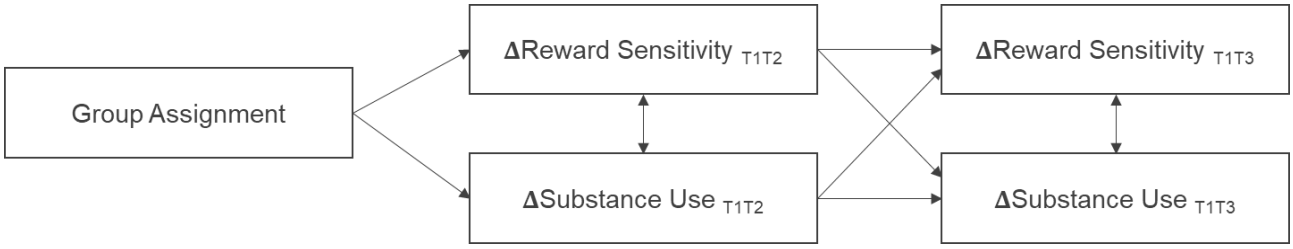
Proposed Path Analysis Model 1 for Hypothesis 2



Note. "ΔReward Sensitivity $_{T1T2}$" refers to the standardized residualized change scores of reward sensitivity measurements between baseline and Week 4. "ΔSubstance Use $_{T1T3}$" refers to the standardized residualized change scores of substance use measurements between baseline and Week 8.

Figure 2

Proposed Path Analysis Model 2 for Hypothesis 2



Note. "ΔReward Sensitivity $_{T1T2}$" refers to the standardized residualized change scores of reward sensitivity measurements between baseline and Week 4. "ΔReward Sensitivity $_{T1T3}$" refers to the standardized residualized change scores of reward sensitivity measurements between baseline and Week 8. "ΔSubstance Use $_{T1T2}$" refers to the standardized residualized change scores of substance use measurements between baseline and Week 4. "ΔSubstance Use $_{T1T3}$" refers to the standardized residualized change scores of substance use measurements between baseline and Week 8.

Power Analysis

For Hypothesis 1, CBTi appears to have a moderate to large effect ($d \geq 0.80$) on reducing insomnia symptoms among individuals with alcohol use or cannabis use when compared to the active control groups (Arnedt et al., 2011; Arnedt et al., 2023). Due to the limited studies on CBTi's effect on reducing substance use, we anticipate a mild to moderate effect of CBTi ($f = 0.25$) on the reduction of insomnia symptoms and substance use in comparing our treatment seeking sample with the control group using ANCOVA. Using G*Power 3.1.9.4, a minimum number of 128 participants will be required for a statistical power of .80 to detect an effect of .25 at an alpha level of .05 (Faul et al., 2009). Considering a drop-out rate of 20%, a total of 154 participants will be required.

For Hypothesis 2, as an exploratory study to investigate the mediating effect of reward sensitivity on the relationship of brief CBTi and substance use, we will conduct analysis using all the samples collected for testing Hypothesis 1. Therefore, a minimum of 154 participants will be required (i.e., 77 participants in brief CBTi group, and 77 participants in Sleep Education group).

Primary and Secondary Outcome

Primary outcome of the study is the effect of brief CBTi on reducing sleep problems (Questionnaires: Insomnia Severity Index, Pittsburgh Sleep Quality Index) and substance

use(Questionnaire: Alcohol Use Disorders Identification Test, Drug Use Disorders Identification Test) after controlling for the treatment effect of Active Control.

Secondary outcome is the mediating effect of reward sensitivity (Questionnaires & Computerized Task: Computerized Iowa Gambling Task, Sensitivity to Reward scales) of in mediating the relationship between Group assignment (CBTi or Active Control) and substance use (Questionnaires: Alcohol Use Disorders Identification Test, Drug Use Disorders Identification Test).

Direct Access to Source Data/Documents

For participants recruited at KCH, IRB / REC, principal investigator and KCH Clinical Psychologists/ Psychology Assistant assigned and approved by direct superior of principal investigator (i.e. SCP) will have access to personal data and study data. Co-investigator from HKU will only have access to de-identified study data (i.e. no full names and HKID number included in the study data).

Data Handling and Record Keeping

Principal investigator will be responsible for safekeeping of the personal and study data during and after the study. Subjects will complete questionnaires in private room for privacy protection. Participants' full names and HKID number will not be written on the questionnaires. For the participants recruited at KCH, hard copies of consent forms and questionnaires will be stored in locked cabinets within hospital premise; soft copies of the consent forms and questionnaires (if any) will be saved in hard drive which is encrypted with passcode and the hard drive will only be kept within hospital premise.

The personal and study data will be kept for 5 years after the study. Afterwards, Personal data will be de-identified (i.e. full names and HKID number will be removed from any collected data). Any hard copies of consent forms and questionnaires will be shredded

and disposed as confidential waste. Soft copies of the consent forms and questionnaires (if any) will be overwritten to ensure permanent deletion.

Financing and Insurance

This study does not receive any sponsor or consume extra resources at Hospital Authority, and no extra funding or cost will be incurred for the study.

Publication Policy

If the research findings are published, it will be submitted to international journals within 5 years after completion of this study. Under no circumstances will the research findings or published articles disclose any participant's personal identity. If participants wish to obtain a copy of the published articles, they may contact the research team using the contact information provided in the consent form.

Ethical Concern

Since sensitive personal information such as substance use will be obtained in the study, data collection will be conducted in private room to protect privacy. All questionnaires will be de-identified to protect confidentiality (i.e. full name and HKID will not be put on questionnaires) and consent form will be kept separately from study questionnaires. Additionally, written consent will be obtained and emphasized in the consent form that participation will be on a voluntary basis and can withdraw any time without penalty.

References

Ahn, W. Y., Busemeyer, J. R., Wagenmakers, E. J., & Stout, J. C. (2008). Comparison of decision learning models using the generalization criterion method. *Cognitive science*, *32*, 1376-1402.

Attkisson, C. C., & Zwick, R. (1982). The Client Satisfaction Questionnaire: Psychometric properties and correlations with service utilization and psychotherapy outcome. *Evaluation and program planning*, *5*, 233-237.

Attkisson, C.C. (2019). The CSQScales Reprint Portfolio. Chicago, IL: Tamalpais Matrix Systems, LLC.

Arnedt, J. T., Conroy, D. A., Armitage, R., & Brower, K. J. (2011). Cognitive-behavioral therapy for insomnia in alcohol dependent patients: a randomized controlled pilot trial. *Behaviour research and therapy*, *49*, 227-233.

Arnedt, J. T., Conroy, D. A., Stewart, H., Yeagley, E., Bowyer, G., Bohnert, K. M., & Ilgen, M. A. (2023). Cognitive behavioral therapy for insomnia to reduce cannabis use: Results from a pilot randomized controlled trial. *Drug and Alcohol Dependence*, *246*, 109835.

Bastien, C. H., Vallières, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep medicine*, *2*, 297-307.

Bart, C. P., Nusslock, R., Ng, T. H., Titone, M. K., Carroll, A. L., Damme, K. S., Young, C. B., Armstrong, C. C., Chein, J., & Alloy, L. B. (2021). Decreased reward-related brain function prospectively predicts increased substance use. *Journal of abnormal psychology*, *130*, 886.

Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2005). Drug use disorders identification test (DUDIT). *European Monitoring Centre for Drugs and Drug Addiction*.

Bishop, T. M., Crean, H. F., Funderburk, J. S., & Pigeon, W. R. (2021). Initial Session effects of brief cognitive behavioral therapy for Insomnia: a secondary analysis of a small Randomized Pilot Trial. Behavioral Sleep Medicine, *19*, 769-782.

Bowirrat, A., & Oscar-Berman, M. (2005). Relationship between dopaminergic neurotransmission, alcoholism, and reward deficiency syndrome. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *132*, 29-37.

Budney, A. J., Hughes, J. R., Moore, B. A., & Vandrey, R. (2004). Review of the validity and significance of cannabis withdrawal syndrome. *American journal of Psychiatry*, *161*, 1967-1977.

Bowen, S., Witkiewitz, K., Clifasefi, S. L., Grow, J., Chawla, N., Hsu, S. H., Carroll, H. A., Harrop, E., Collins, S. E., Lustyk, M. K., & Larimer, M. E. (2014). Relative efficacy of mindfulness-based relapse prevention, standard relapse prevention, and treatment as usual for substance use disorders: a randomized clinical trial. *JAMA psychiatry*, *71*, 547-556.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research*, *28*, 193-213.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of personality and social psychology*, *67*, 319.

Chakravorty, S., Vandrey, R. G., He, S., & Stein, M. D. (2018). Sleep management among patients with substance use disorders. *Medical Clinics*, *102*, 733-743.

Chan, WHJ (2022). Tai Po Hospital, Hospital Authority, Hong Kong.

Chaudhary, V., Katyal, R., Singh, S. P., Joshi, H. S., Upadhyay, D., & Singh, A. (2015). A study on pattern of alcohol use using AUDIT among the college students in a

medical college of North India. *National Journal of Community Medicine*, *6*, 253-257.

Cheung, C. (1987). Follow-up study of examination stress on health of adolescents in Taiwan. *Chinese Journal of Psychology*, *9*.

Conroy, D. A., & Arnedt, J. T. (2014). Sleep and substance use disorders: an update. *Current psychiatry reports*, *16*, 1-9.

Copersino, M. L., Boyd, S. J., Tashkin, D. P., Huestis, M. A., Heishman, S. J., Dermand, J. C., Simmons, M. S., & Gorelick, D. A. (2006). Cannabis withdrawal among non-treatment-seeking adult cannabis users. *The American Journal on Addictions*, *15*, 8-14.

de Meneses-Gaya, C., Zuardi, A. W., Loureiro, S. R., & Crippa, J. A. S. (2009). Alcohol Use Disorders Identification Test (AUDIT): An updated systematic review of psychometric properties. *Psychology & Neuroscience*, *2*, 83.

Dugré, J. R., Orban, P., & Potvin, S. (2023). Disrupted functional connectivity of the brain reward system in substance use problems: A meta-analysis of functional neuroimaging studies. *Addiction Biology*, *28*.

Ellis, J. G., Cushing, T., & Germain, A. (2015). Treating acute insomnia: a randomized controlled trial of a "single-shot" of cognitive behavioral therapy for insomnia. *Sleep*, *38*(6), 971-978.

Fadhel, F. H. (2020). Exploring the relationship of sleep quality with drug use and substance abuse among university students: a cross-cultural study. *Middle East Current Psychiatry*, *27*, 65.

Freeman, L. K., & Gottfredson, N. C. (2018). Using ecological momentary assessment to assess the temporal relationship between sleep quality and cravings in individuals recovering from substance use disorders. *Addictive Behaviors*, *83*, 95-101.

Fridberg, D. J., Queller, S., Ahn, W. Y., Kim, W., Bishara, A. J., Busemeyer, J. R., Porrino, L., & Stout, J. C. (2010). Cognitive mechanisms underlying risky decision-making in chronic cannabis users. *Journal of mathematical psychology*, *54*(1), 28-38.

Goldberg, D. P., Oldehinkel, T., & Ormel, J. (1998). Why GHQ threshold varies from one place to another. *Psychological medicine*, *28*, 915-921.

Goldberg, D.P. & Hillier, V.F. (1979). A scaled version of the General Health Questionnaire. *Psychological Medicine, 9,* 139-45.

Grant, S., Contoreggi, C., & London, E. D. (2000). Drug abusers show impaired performance in a laboratory test of decision making. *Neuropsychologia*, *38*, 1180-1187.

Grau-López, L., Daigre, C., Grau-López, L., Rodriguez-Cintas, L., Egido, Á ., Casas, M., & Roncero, C. (2016). Administrative prevalence of insomnia and associated clinical features in patients with addiction during active substance use. *Actas espanolas de psiquiatria*, *44*, 64–71.

Gray, J. A. (1987). *The Psychology of Fear and Stress*. Cambridge University Press.

Guo, R., Vaughan, D. T., Rojo, A. L. A., & Huang, Y. H. (2023). Sleep-mediated regulation of reward circuits: implications in substance use disorders. *Neuropsychopharmacology*, *48*(1), 61-78.

Gunn, H. E., Tutek, J., & Buysse, D. J. (2019). Brief behavioral treatment of insomnia. *Sleep medicine clinics*, *14* 235-243.

Hasler, B. P., Soehner, A. M., & Clark, D. B. (2014). Circadian rhythms and risk for substance use disorders in adolescence. *Current opinion in psychiatry*, *27*, 460-466.

Hildebrand, M. (2015). The psychometric properties of the drug use disorders identification test (DUDIT): a review of recent research. *Journal of substance abuse treatment*, *53*, 52-59.

Kwon, M., Wang, J., Wilding, G., Dickerson, S. S., & Dean, G. E. (2022). Brief behavioral treatment for insomnia: a meta-analysis. *Behavioral sleep medicine*, *20*, 674-694.

Joyner, K. J., Bowyer, C. B., Yancey, J. R., Venables, N. C., Foell, J., Worthy, D. A., Hajcak, G., Bartholow, B. D., & Patrick, C. J. (2019). Blunted reward sensitivity and trait disinhibition interact to predict substance use problems. *Clinical Psychological Science*, *7*, 1109-1124.

Kelly, J. F., Bergman, B. G., Hoeppner, B. B., Vilsaint, C., & White, W. L. (2017). Prevalence and pathways of recovery from drug and alcohol problems in the United States population: Implications for practice, research, and policy. *Drug and alcohol dependence*, *181*, 162-169.

Kim, S. H., Yoon, H., Kim, H., & Hamann, S. (2015). Individual differences in sensitivity to reward and punishment and neural activity during reward and avoidance learning. *Social cognitive and affective neuroscience*, *10*, 1219-1227.

Kolla, B. P., Mansukhani, M. P., Biernacka, J., Chakravorty, S., & Karpyak, V. M. (2020). Sleep disturbances in early alcohol recovery: Prevalence and associations with clinical characteristics and severity of alcohol consumption. *Drug and Alcohol Dependence*, *206*, 107655.

Koob, G. F. (1992). Drugs of abuse: anatomy, pharmacology and function of reward pathways. *Trends in pharmacological sciences*, *13*, 177-184.

Koob, G. F., & Volkow, N. D. (2016). Neurobiology of addiction: a neurocircuitry analysis. *The Lancet Psychiatry*, *3*, 760-773.

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: an integrative quantitative model of the adult externalizing spectrum. *Journal of abnormal psychology*, *116*, 645.

Larsen, D. L., Attkisson, C. C., Hargreaves, W. A., & Nguyen, T. D. (1979). Assessment of client/patient satisfaction: development of a general scale. *Evaluation and program planning*, *2*, 197-207.

Li, C. S. R., Huang, C. Y., Lin, W. Y., & Sun, C. W. V. (2007). Gender differences in punishment and reward sensitivity in a sample of Taiwanese college students. *Personality and Individual Differences, 43*, 475–483

Ling, J., Lin, X., Li, X., Chan, N. Y., Zhang, J., Wing, Y. K., Hu, X., & Li, S. X. (2022). Neural response to rewards in youths with insomnia. *Sleep, 45*.

Liu, S. G. B. T. (2019). A Multilevel Analysis of the Demography of Drug Abuse in Hong Kong. Narcotics Division of Hong Kong. Retrieved from https://www.nd.gov.hk/pdf/BDF%20170062%20Full%20Report_en.pdf.

McHugh, R. K., Hearon, B. A., & Otto, M. W. (2010). Cognitive behavioral therapy for substance use disorders. *Psychiatric Clinics*, *33*, 511-525.

McNeely, J., Wu, L. T., Subramaniam, G., Sharma, G., Cathers, L. A., Svikis, D., Sleiter, L., Russell, L., Nordeck, C., Sharma, A., O'Grady, K. E., Bouk, L. B., Cushing, C., King, J., Wahle, A., & Schwartz, R. P. (2016). Performance of the tobacco, alcohol, prescription medication, and other substance use (TAPS) tool for substance use screening in primary care patients. *Annals of internal medicine*, *165*, 690-699.

Mijnster, T., Boersma, G. J., Meijer, E., & Lancel, M. (2022). Effectivity of (personalized) cognitive behavioral therapy for insomnia in mental health populations and the elderly: An overview. *Journal of personalized medicine*, *12*, 1070.

Miller, M. B., Freeman, L. K., Helle, A. C., Hall, N. A., DiBello, A. M., & McCrae, C. S. (2023). Comparative feasibility and preliminary efficacy of CBT for insomnia among adults seeking and not seeking addiction treatment. *Journal of Sleep Research*.

Mitchell, M. D., Gehrman, P., Perlis, M., & Umscheid, C. A. (2012). Comparative effectiveness of cognitive behavioral therapy for insomnia: a systematic review. *BMC family practice*, *13*, 1-11.

Motomura, Y., Katsunuma, R., Ayabe, N., Oba, K., Terasawa, Y., Kitamura, S., Moriguchi, Y., Hida, A., Kamei, Y., & Mishima, K. (2021). Decreased activity in the reward network of chronic insomnia patients. *Scientific reports*, *11*, 3600.

Mullin, B. C., Phillips, M. L., Siegle, G. J., Buysse, D. J., Forbes, E. E., & Franzen, P. L. (2013). Sleep deprivation amplifies striatal activation to monetary reward. *Psychological medicine*, *43*, 2215-2225.

Nejtek, V. A., Kaiser, K. A., Zhang, B., & Djokovic, M. (2013). Iowa Gambling Task scores predict future drug use in bipolar disorder outpatients with stimulant dependence. *Psychiatry Research*, *210*, 871-879.

Ong, J. C., Kuo, T. F., & Manber, R. (2008). Who is at risk for dropout from group cognitive-behavior therapy for insomnia? *Journal of psychosomatic research*, *64*, 419-425.

Pasch, K. E., Latimer, L. A., Cance, J. D., Moe, S. G., & Lytle, L. A. (2012). Longitudinal bi-directional relationships between sleep and youth substance use. *Journal of youth and adolescence*, *41*, 1184-1196.

Perlis, M. L., Jungquist, C., Smith, M. T., & Posner, D. (2005). *Cognitive behavioral treatment of insomnia: A session-by-session guide* (Vol.1). Springer Science & Business Media.

Pujara, M. S., Philippi, C. L., Motzkin, J. C., Baskaya, M. K., & Koenigs, M. (2016). Ventromedial prefrontal cortex damage is associated with decreased ventral striatum volume and response to reward. *Journal of Neuroscience*, *36*, 5047-5054.

Reinert, D. F., & Allen, J. P. (2007). The alcohol use disorders identification test: an update of research findings. *Alcoholism: Clinical and Experimental Research, 31*, 185-199.

Roane, B. M., & Taylor, D. J. (2008). Adolescent insomnia as a risk factor for early adult depression and substance abuse. *Sleep, 31,* 1351-1356.

Robinson, R. G., & Price, T. R. (1982). Post-stroke depressive disorders: a follow-up study of 103 patients. *Stroke, 13,* 635-641.

Rosenblum, M. (2017). Substance abuse and insomnia. *Minnesota medicine*, *100*(3), 38-39.

Sakakibara, B. M., Miller, W. C., Orenczuk, S. G., & Wolfe, D. L. (2009). A systematic review of depression and anxiety measures used with individuals with spinal cord injury. *Spinal cord, 47,* 841-851.

Saunders, J. B., Aasland, O. G., Babor, T. F., De la Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction, 88,* 791-804.

Short, N. A., Zvolensky, M. J., & Schmidt, N. B. (2021). A pilot randomized clinical trial of Brief Behavioral Treatment for Insomnia to reduce problematic cannabis use among trauma-exposed young adults. *Journal of substance abuse treatment*, *131,* 108537.

Speed, T. J., Hanks, L., Turner, G., Gurule, E., Kearson, A., Buenaver, L., Smith., M. T., & Antoine, D. (2022). A comparison of cognitive behavioral therapy for insomnia to standard of care in an outpatient substance use disorder clinic embedded within a therapeutic community: a RE-AIM framework evaluation. *Trials, 23,* 965.

Stein, M. D., Herman, D. S., Bishop, S., Lassor, J. A., Weinstock, M., Anthony, J., & Anderson, B. J. (2004). Sleep disturbances among methadone maintained patients. *Journal of substance abuse treatment, 26,* 175-180.

Taylor, D. J., Wilkerson, A., Hryshko-Mullen & Goodie, J. L, (2019). *Cognitive-behavioral therapy for insomnia in the military: Rating scales.*

Tsai, Pei-Shan, Wang, Shu-Yi, Wang, Mei-Yeh, Su, Chein-Tien, Yang, Tsung-Tsair, Huang, Chun-Jen, & Fang, Su-Chen. (2005). Psychometric evaluation of the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) in primary insomnia and control subjects. *Qual Life Res, 14,* 1943-1952.

Volkow, N. D., & Blanco, C. (2023). Substance use disorders: a comprehensive update of classification, epidemiology, neurobiology, clinical aspects, treatment and prevention. *World Psychiatry*, *22*, 203-229.

Volkow, N. D., Wang, G. J., Fowler, J. S., Tomasi, D., Telang, F., & Baler, R. (2010). Addiction: decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. *Bioessays*, *32*, 748-755.

Yang, C. M., Hsu, S. C., Lin, S. C., Chou, Y. Y., & Chen, Y. M. (2009). Reliability and validity of the Chinese version of insomnia severity index. *Arch Clin Psychol*, *4*, 95-104.