



Full length article

# Does abstinence resolve poor sleep quality in former methamphetamine dependents? <sup>☆</sup>



Amir Rezaei Ardani, Seyyed Ali Saghebi, Mahsa Nahidi, Farzaneh Zeynalian\*

Psychiatry and Behavioural Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

## ARTICLE INFO

### Keywords:

Sleep quality  
Amphetamine  
Abstinence  
Depression  
Anxiety

## ABSTRACT

**Background and objective:** Among substances that have a significant effect on sleep are stimulants, including amphetamines. As there are few studies assessing sleep quality in methamphetamine withdrawal this study aims to evaluate changes in sleep quality of methamphetamine dependent patients during early remission period by controlling depression and anxiety as confounding variables.

**Methods:** This study was conducted in Mashhad, Iran. Ninety amphetamine dependent patients, who were admitted in residential centers during 2012–2014 and met our inclusion criteria, were chosen by purposive nonprobability sampling method. Sleep quality was assessed by Pittsburg sleep questionnaire, in the first, second, and after the fourth week of abstinence. Additionally all participants were assessed by Beck Depression Inventory-2 and Beck Anxiety Inventory for controlling depressive and anxiety symptoms.

**Results:** The prevalence of improper quality of sleep was very high (97.8%) within the first week of withdrawal, but it reduced considerably four weeks after abstinence (52.2%), which was statistically significant ( $P=0.00$ ). The variations of depression and anxiety levels within four weeks after quitting methamphetamine, have low impact on variation of patients' sleep quality (adjusted  $R^2 < 0.5$ ). Furthermore, the effectiveness of these two intervening variables on patients' quality of sleep was dwindled over time after abstinence.

**Conclusions:** This study showed that the patients' quality of sleep improved significantly four weeks after abstinence and its variation was independent from variations in anxiety and depressive symptoms.

## 1. Introduction

Sleep disorders have a significant role in the general and clinical health of the society [1]. They could be an independent clinical disorder or a symptom of a clinical syndrome. They usually have direct and indirect effects on the daily functioning and quality of life of sufferer and could lead to significant healthcare costs for the society [2–5]. Each year they affect many individuals and cause intrapersonal and interpersonal impairments [6]. To date, many studies have focused to find out probable etiologies of sleep disturbances and they have shown us the significant correlation between sleep disorders and substance use [7–9]. Among the substances which have a significant effect on the sleep condition are stimulants, including amphetamines [10]. Amphetamines are used for curbing the appetite, increasing attention and concentration, increasing energy and also as an illicit recreational substance [11,12].

It seems that the effect of stimulants on the sleep-wake cycle is fully discussed in the literature. However, our knowledge has mainly derived from the studies performed on the stimulant medications (e.g. methyl-

phenidate) or cocaine; and what is said about the effects of amphetamines on sleep-wake cycle is basically generalization of the results of studies which have been done on the other drugs [13]. Nevertheless there are several reasons that amphetamine and amphetamine-like drugs, especially methamphetamine, have differently influenced the consumers. Amphetamines are known to have longer half-life (9–15 h) in comparison to other stimulants [14]. They have proven neurotoxic effects through reactive oxygen species and hyperthermia, causing axonal injury, especially in synaptic terminals [15,16]. They also lead to significant changes in neurotransmission of glutamate, dopamine, serotonin and norepinephrine causing major behavioral changes [17–20]. Therefore, independent assessment of neurological and psychological alteration of brain activity in methamphetamine abusers is warranted.

According to few researches to reveal the effects of amphetamines on sleep-wake cycle, it has been suggested that consuming amphetamines usually leads to insomnia immediately after usage [10]. It can also lead to hypersomnia in the early withdrawal states [21]. In 1960s Rechtschaffen et al. showed that a small amount of amphetamine can

Peer review under responsibility of Brazilian Association of Sleep.

\* Corresponding author.

E-mail address: [aminzadeh.b@gmail.com](mailto:aminzadeh.b@gmail.com) (F. Zeynalian).

<http://dx.doi.org/10.1016/j.slsci.2016.11.004>

Received 8 September 2016; Received in revised form 16 October 2016; Accepted 21 November 2016

Available online 30 November 2016

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increase sleep latency and decrease REM sleep [22]. Withdrawal from amphetamine, on the other hand, can lead to increased REM sleep, lasting for several days [23]. Later in 1990s, Mitler et al. reported same results and showed that methamphetamine can decrease sleep efficiency in low doses (10 mg) [24], although sleep increases for 3–5 days after withdrawal [23]. But other studies brought us more confusing findings. There are also reports of delayed insomnia in users attempting to quit long-term amphetamine use after the 3–5 initial days [23]. Furthermore, the impact of anxiety and depression on sleep quality is not negligible. Stimulants often accompany with anxiety states short after consuming and depressive states in long term use, while patients usually develop depressive symptoms short after quitting them [25]. According to frequent reports, depression and anxiety could have deteriorating effects on sleep quality [26,27]. Therefore, sleep quality of patients who stop using methamphetamines, simply could influence by changes in perceived anxiety or depression. Unfortunately there have not been adequate studies on sleep disorders in amphetamine users.

Considering the importance of sleep health, many studies have examined sleep quality as a marker of general health [28]. Sleep quality, which is a self evaluation of sleep, is considered more important than sleep quantity in the assessment of general health [29,30]. Poor sleep quality is associated with fatigue and impaired mental and occupational functions [31]. This index is affected by many sleep-wake cycle disorders and studies have shown that stimulants affect sleep quality as well [32]. As there are not enough studies assessing sleep quality in methamphetamine dependent patients during prolonged abstinence, especially after prolonged use [33]; the present study aims to evaluate subjective changes in sleep quality of methamphetamine dependent patients during early remission period.

## 2. Methods

### 2.1. Subjects

The present study was designed in cross-sectional fashion and was performed in Mashhad City during 2012–2014. Mashhad is the second largest city in Iran, with a population of more than three million people. According to national strategies for treatment of substance use disorder in Iran, there are some residential centers for the treatment of substance use disorders which admit volunteers for almost 3 months. Although individual or group supportive psychotherapies and over-the-counter (OTC) medications are offered in these residential centers, patients have no access to any kind of substances and relapse is prevented in the initial phases of withdrawal, when craving is at its highest. Therefore, patients experience abstinence in these controlled environments during institutionalization. Since there is no psychiatric medication in these residential programs, patients with significant mood and anxiety symptoms, ideas of harm to self or others, intoxication, and psychotic disorders are not allowed to be admitted and are referred to other type of outpatient or inpatient treatment centers. As there is no need for specific pharmacotherapy in the treatment of amphetamine dependence disorder [14], these centers present an opportunity for researchers to evaluate patients, who do not require any kind of pharmacotherapy, for long periods after reaching abstinence. This study was performed in collaboration of participants of these residential centers in Mashhad.

### 2.2. Procedure

After explaining the project to patients at the beginning of admission to the residential centers, every patient who consented to participate in the study, went through a psychiatric interview to be assessed for the inclusion criteria. Then sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI). According to McGregor et al. the methamphetamine withdrawal time-course could be divided into acute

(first 7–10 days) and sub-acute (11th–21st days) phases [34]; so, the initial assessment of sleep quality was done in the first week of initiation of withdrawal (before day 3) to rate sleep quality in the acute phase, the second assessment was done in the second week (days 11–14) to rate sleep quality in the sub-acute phase, and the last assessment was done after the 4th week (days 28–35) of abstinence, to rate sleep quality in the primary remission period (according to DSM-IV-TR criteria).

Participants of the study were screened by two trained interviewers (a psychiatrist and a psychologist) by means of structural interviewing. The inclusion criteria was age between 18 and 60 years-old, normal IQ (over 100), methamphetamine dependence disorder according to DSM-IV-TR criteria, no comorbid dependence on other substances except nicotine (occasional abuse of alcohol, opioids, benzodiazepines, cannabis to the extent not warranting a diagnosis of dependency according to DSM-IV-TR was acceptable), not taking medications affecting sleep-wake cycle (in this study, antihistamines among OTCs), no methamphetamine induced disorder other than sleep disorder, no comorbid axis I psychiatric disorder (unrelated to methamphetamine use), and no medical condition affecting sleep. Every patient who fulfilled the inclusion criteria and accepted the written informed consent could participate in the study, so the sampling method was purposive nonprobability sampling. Participants opting to quit the study or the ones discharged before the third assessment were excluded from the study. Sampling was started from March 2012 to August 2014. During this period of time, ninety patients completed the study. Considering the high comorbidity of depressive and anxiety symptoms with sleep disorders [35,36], probable high rates of depressive and anxiety symptoms in the first days of joining to any residential program and also the high frequency of these symptoms in the initial phase of withdrawal from stimulants [34], all participants were given Beck Depression Inventory II (BDI-II) and Beck Anxiety Inventory (BAI) in addition to PSQI for controlling the anxiety and depressive symptoms as confounding variables. All questionnaires were anonymous to prevent any disclosure of personal information and participants were identified with an anonymous number assigned to their profile.

### 2.3. Instruments

The questionnaires used in this study were:

#### 2.3.1. Pittsburgh Sleep Quality Index (PSQI)

Sleep quality is affected by several factors, and these factors significantly differ in different individuals. Therefore, it seems that a self-report questionnaire is best fitted to assess sleep disorders [3,37]. The PSQI has 7 components and the sum of their scores make the global PSQI score. The participant score the questionnaire on a likert scale from 0 (best condition) to 3 (worst condition), so the minimum score is 0 and the maximum is 21. A global PSQI score over 5 is associated with poor sleep quality. This questionnaire has been studied in various populations and its score is moderately to highly correlate with the sleep quality reported by the patients [38–41].

#### 2.3.2. Beck Depression Inventory-II (BDI-II)

This is a self-report 21-item questionnaire which assesses depressive symptoms. The total score range is from 0 to 63, the higher scores representing a more severe depression. This questionnaire has a high validity in all populations and in depressed and non-depressed individuals which has been reported 0.70–0.90 in different studies [42,43].

#### 2.3.3. Beck Anxiety Inventory (BAI)

Beck Anxiety Inventory is a 21-item questionnaire, assessing the anxiety state of individuals. The total scores range from 0 to 63, higher scores indicating a more severe anxiety. The validity of this scale has

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