The nature, time course and severity of methamphetamine withdrawal

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ABSTRACT

Aims To characterize the natural history of methamphetamine withdrawal during the first 3 weeks of abstinence.

Design Cross-sectional study with comparison group.

Setting A substance use treatment facility in Chiang Mai Province, Thailand.

Participants The sample comprised 21 in-patients undergoing treatment for methamphetamine dependence. Nine age- and sex-matched non-dependent individuals provided comparison data.

Measurements Instruments including: the Amphetamine Withdrawal Questionnaire, a modified version of the Cocaine Selective Severity Assessment, Clinical Global Impression scale and the St Mary's Hospital Sleep Questionnaire were completed daily for the first 3 weeks of abstinence.

Findings Methamphetamine withdrawal severity declined from a high initial peak within 24 hours of the last use of amphetamines reducing to near control levels by the end of the first week of abstinence (the acute phase). The acute phase of amphetamine withdrawal was characterized by increased sleeping and eating, a cluster of depression-related symptoms and less severely, anxiety and craving-related symptoms. Following the acute withdrawal phase most withdrawal symptoms remained stable and at low levels for the remaining 2 weeks of abstinence.

Conclusions This study has provided evidence of a methamphetamine withdrawal syndrome that can be categorized into two phases, the acute phase lasting 7–10 days during which overall symptom severity declined in a linear pattern from a high initial peak, and a subacute phase lasting at least a further 2 weeks.

KEYWORDS Abstinence, in-patient, methamphetamine, sleep, withdrawal.

INTRODUCTION

The problem of illicit psychostimulant use is now a global one. Internationally, the most widely abused illicit drug is cannabis followed, according to region, by amphetamine-type stimulants or cocaine [1]. Despite the widespread illicit use of amphetamines and the substantial problems associated with their use [2], until recently few users sought help from treatment agencies. The reluctance to access treatment may be due to a perception that treatment agencies and programmes have developed to meet the needs of opioid users and have little to offer methamphetamine users seeking to modify their drug use [3].

Failure to manage methamphetamine withdrawal symptoms during treatment may contribute to the high rates of relapse in the first days or weeks post-cessation [4]. An important first step in the development of effective treatment is the mapping of the time course and severity

of methamphetamine withdrawal symptoms. This information would facilitate the timely administration of appropriate interventions aimed at specific symptoms.

Although the existence of an amphetamine dependence syndrome has been established [5–7], there is a paucity of evidence-based information on which to base effective treatments [8], particularly in comparison to other drugs of dependence. Amphetamine withdrawal has been studied extensively in animals [9]; however, the majority of human studies have been retrospective [10,11], they have used small sample numbers [12,13] or the subjects were withdrawing from multiple substances [14–17]. Two retrospective studies of amphetamine users identified a wide range of withdrawal symptoms [6,7]. Many of these symptoms were consistent with those experienced in opioid withdrawal. This may have been a function of the questionnaire used, the Severity of Amphetamine Dependence Questionnaire (SAmDQ), which is based on an opiate dependence questionnaire.

Only one study has examined systematically amphetamine withdrawal symptoms over time. Amineptine was compared to placebo in a randomized design [18]. In comparison to controls, the amineptine group showed significant reductions in three symptoms, fatigue, increased appetite and craving for sleep at the end of the first and second week of treatment. While these results were encouraging, amineptine has since been withdrawn due to reports of abuse. Withdrawal symptoms in this study were measured at only three time-points 1 week apart. Additionally, assessment time-points were determined by the time of admission for in-patient treatment rather than being anchored to the time of last amphetamine use.

Depressive symptoms, a core criterion for the diagnosis of cocaine or amphetamine withdrawal [19], are substantially higher in stimulant-dependent individuals than in the general community [20] and are commonly identified in treatment samples of amphetamine users [10,21]. In an early series of case studies, four 'moderate' amphetamine users all experienced depression that peaked at 48–72 hours following the last amphetamine dose [12]. Further, depression in some methamphetamine users may persist for several years after treatment even where substance use is reduced [22].

There are also clinical reports of an initial 'crash' period of around 3 days following the cessation of amphetamine use. The crash phase, during which the individual may sleep for much of the time, may be followed by a prolonged period of insomnia. Gossop and colleagues investigated sleep duration in hospitalized amphetamine users [23]. This study showed that hours of sleep for amphetamine users were greater than or similar to controls on nights 1–5 but that amphetamine users slept comparatively less on nights 6–20 when the study ended. These data do not provide support for clinical reports of a 'crash' following cessation of amphetamine use, rather an initial period of 'normal' sleep followed by a prolonged period (at least 15 days) of relative insomnia. Although this study yielded valuable information on the sleep patterns of amphetamine users in the initial 3 weeks of abstinence, no data on the intensity or frequency of amphetamine use were reported and no other withdrawal symptoms were measured.

The natural history of amphetamine withdrawal is still poorly understood, despite a small number of studies which have provided limited information on withdrawal symptoms over time [12,23,24]. The recent failure of an exhaustive review of the literature to find any studies describing the natural history of amphetamine withdrawal points to the need for empirical data in this area [25].

Aim

The aim of this study is to provide quantitative information on the natural history of amphetamine withdrawal through the identification and systematic measurement of signs and symptoms occurring during the first 3 weeks of abstinence from amphetamines.

METHOD

The study was conducted at the Northern Drug Dependence Treatment Centre (NDDTC), a substance use treatment facility in Chiang Mai Province, Thailand. Consecutive admissions to NDDTC for treatment of methamphetamine dependence were assessed for consistency with the selection criteria. In-patient participants included in the sample were aged between 18 and 45 years, had urine positive for amphetamines at admission and fulfilled the *Diagnostic and Statistical Manual* version IV (DSM-IV) criteria for amphetamine dependence [19]. Patients with an acute medical or psychiatric illness requiring psychotropic medication or who fulfilled the DSM-IV diagnostic criteria for other substance dependence, except nicotine, were excluded. To confirm abstinence from amphetamines, a urine drug screen was conducted at weekly intervals. Urine was analysed by cloned enzyme donor immunoassay using a cut-off level of 1000 ng/ml.

To provide comparison data, a group of nine age- and sex-matched (non-dependent) healthy individuals from the same geographical area completed the same withdrawal and sleep questionnaires over the same time period. Five comparison group members were recruited from among staff at the clinic (e.g. security staff, clerical officers). The remaining four were medical students

studying at Chiang Mai University. Suitable comparison group members were approached individually by a member of the research team and invited to participate. There were no refusals and no compensation was offered for study participation.

Data were collected between October and December 2002. Participants gave written informed consent prior to study entry and there was no compensation for study participation. None of the patients were mandated for treatment and a family member referred almost all for treatment. Of the 21 in-patient participants, two received 5 mg of diazepam on one occasion and one 10 mg of diazepam on one occasion for insomnia. No other medications were administered. All in-patient participants received a B-complex vitamin daily and took part in the group and occupational therapy programme that is a normal part of in-patient treatment for methamphetamine dependence and withdrawal at NDDTC. Patients undergoing treatment for methamphetamine withdrawal were housed in two large open wards that could accommodate up to 65 people. Although the campus was secure and visitors monitored, patients had access to gardens and outdoor recreation and dining areas. Ethics approval for the study was received from the Ministry of Public Health in Thailand and the Ethics Committee of the University of Adelaide, Australia.

Once informed consent was obtained, a structured interview assessing demographic data, drug use and treatment history was administered. The Severity of Dependence Scale [26] was completed on admission to measure severity of dependence on amphetamines.

Two instruments were used to measure methamphetamine withdrawal. The Amphetamine Withdrawal Questionnaire (AWQ) [24], based on the DSM-IV criteria for amphetamine withdrawal, is a 10-item, self-completed instrument designed to measure the domains of craving, dysphoria, anhedonia, increased appetite, fatigue, agitation, anxiety, increased sleep, vivid, unpleasant dreams and slowing of movement over the previous 24 hours. Items were scored on a four-point Likert-type scale, from 0 (not at all) to 4 (very much).

A modified version of the Cocaine Selective Severity Assessment scale (CSSA) [27] was used to provide information on a broader range of symptoms than that assessed by the AWQ. The interviewer-administered CSSA is a reliable and valid measure of cocaine abstinence symptoms. Given that the DSM-IV lists the same symptoms for cocaine and amphetamine withdrawal, it was considered that this scale could be modified for use in amphetamine withdrawal. Modification of the CSSA involved replacing 'cocaine' with 'amphetamine' to produce the Amphetamine Selective Severity Assessment scale (ASSA). Domains assessed by this 18-item scale included those addressed by the AWQ (with the exception of psychomotor retardation, agitation and vivid dreams) plus decreased appetite and sleep, craving for carbohydrate (including craving for sweet food and/or drinks), bradycardia, concentration, irritability, paranoid and suicidal ideation, tension and inactivity (range = 0–7, higher scores indicated greater severity).

The St Mary's Hospital Sleep Questionnaire (SMHSQ) [28] was administered daily to assess sleep characteristics on the previous night. This self-report questionnaire has shown satisfactory reliability for use with psychiatric and medical in-patients [28,29]. Domains assessed by the SMHSQ include hours of night and daytime sleep, sleep depth, quality of sleep, sleep satisfaction, clearheadedness on arising, number of awakenings during the night and sleep latency.

Depression was measured via the Beck Depression Inventory ll (BDI) [30], a widely used measure of current depression. The BDI was administered on admission and at the beginning of weeks 2 and 3 of in-patient treatment.

To provide an observer-rated measure of withdrawal, nursing staff completed the Clinical Global Impressions (CGI) scale daily [31]. Blood pressure and radial pulse were recorded daily for each in-patient participant.

Data were collected for 21 days (the standard duration of treatment for acute amphetamine withdrawal at the time the study was conducted) following the last use of amphetamines. Measures (i.e. ASSA, AWQ, SMHSQ and CGI) were completed once daily. Data were collated according to the time since last use; that is, data collected within 24 hours of the last use of methamphetamine was designated 'day 0'; data collected 24–48 hours following the last use of methamphetamine was called 'day 1', etc.

Analyses

Changes over time and differences between groups were measured using a linear mixed model ANOVA with day of abstinence (for subjects) or data collection (for the comparison group) as the fixed factor. Pearson's correlation coefficient was used to identify relationships between normally distributed continuous variables. Alpha level was set at 0.05 and confidence intervals of 95% used. All analyses were conducted using SPSS version 11.5 for Windows.

RESULTS

Of 72 patients who were admitted for treatment of amphetamine dependence during the study period, three declined to participate, 11 were currently experiencing auditory hallucinations, eight had concurrent dependence on alcohol, 14 were under 18 years of age and 15 provided a urine sample negative for amphetamines. The

Table 1 Characteristics of the study sample.

Characteristics	(n = 21)
Age; mean years (range)	21.4 (18–28)
Male n (%)	20 (95)
Unemployed n (%)	16 (76)
Unmarried n (%)	20 (95)
Education	
Secondary n (%)	14 (67)
Vocational/trade school n (%)	6 (29)
University n (%)	1 (5)
Age first used amphetamine; mean years (range)	17 (11–25)
Length of regular amphetamine use; mean years (range)	4 (1–15)
Amount (tablets) used per day in the previous month, median (range)	2.5 (1–8)
Amount (Thai Baht*) spent per day on methamphetamines, median (range)	200 (70.00–850.0)
Previous treatment for amphetamine dependence, n (%)	6 (29)
Severity of Dependence Scale, mean (range)	6.2 (2–11)

*At the time of the study exchanges rates were: Thai Baht 42.44 = US$1 and Thai Baht 41.82 = €1.

final sample comprised 21 in-patient participants, five of whom provided data on day 0; 12 on day 1; 18 on days 2 and 3; 19 on days 4–9; 18 on days 10–14; 16 on days 15–17 and 15 on days 18–20. Table 1 shows the characteristics of the study sample.

Only one female participated in the study and few had a partner at the time of entering treatment. The majority had completed secondary education and were currently unemployed. For all in-patient participants, amphetamines were administered by heating methamphetamine tablets (usually on a piece of foil) and then inhaling the fumes. Of the 21 in-patients, 17 (81%) had a clinically significant dependence on amphetamines [32].

Treatment retention

The mean number of days on which in-patient participants remained in the study was 17.9 (SEM = 1.7) range: 3–21 days. Of the 21 in-patients enrolled in the study, four left the clinic prior to completing treatment, two developed auditory hallucinations requiring acute treatment and were withdrawn from the study and 15 completed methamphetamine withdrawal treatment.

Amphetamine withdrawal: summary scores

Figure 1 shows the pattern of withdrawal symptoms measured by the three withdrawal instruments, the self-
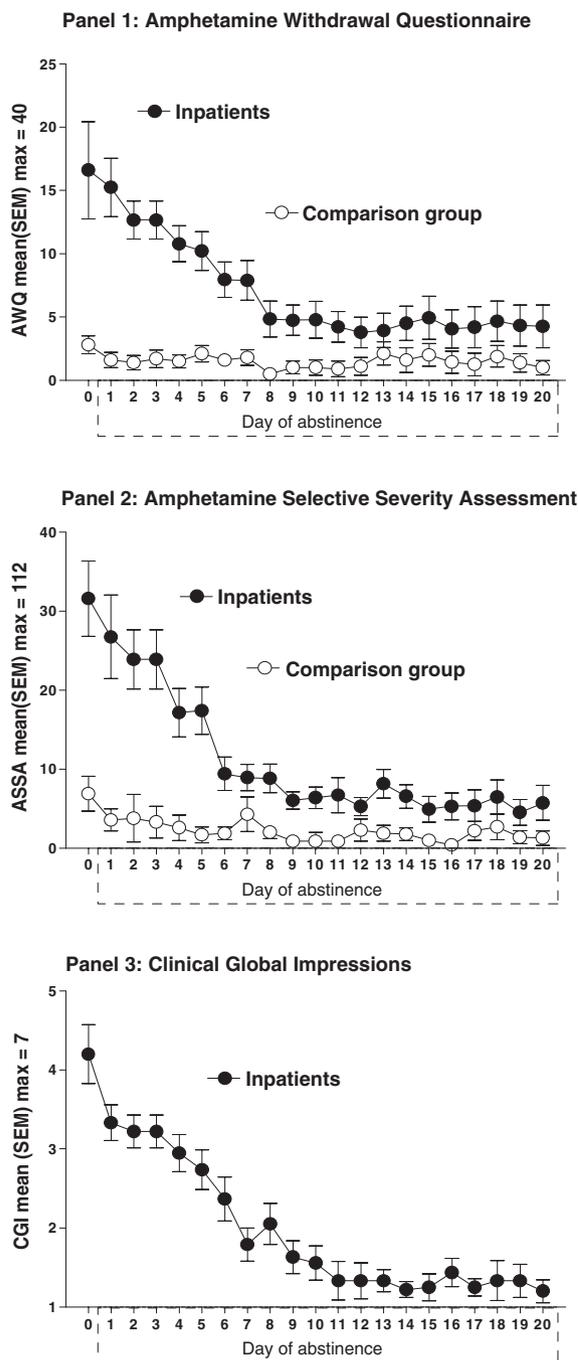
Figure 1 Amphetamine withdrawal symptoms

completed AWQ (panel 1), the interviewer-administered ASSA (panel 2) and the observer-rated CGI (panel 3). For in-patients, AWQ scores reduced significantly over the first 3 weeks of abstinence ($F = 3.5$, df 20,475, $P < 0.001$). There were significant differences in AWQ scores between in-patients and the comparison group ($F = 144.6$, df 1,475, $P < 0.001$) and a significant interaction effect of time (day of abstinence) and group ($F = 2.4$, df 20,475, $P = 0.003$).

Similarly, there was a significant reduction in withdrawal discomfort as measured by the ASSA over the first 3 weeks of abstinence ($F = 5.7$, df 20,476, $P < 0.001$). Significant differences between in-patients and the comparison group were revealed ($F = 117.6$, df 1,476, $P < 0.001$), as was a significant interaction effect of time and group ($F = 3.8$, df 20,476, $P < 0.001$). Reliability analysis (Cronbach's alpha) of the modified CSSA showed satisfactory internal consistency (0.80) that compared favourably with reliability analysis for the AWQ (0.90).

The pattern of CGI scores was similar to that shown for the AWQ and the ASSA, reducing significantly over the first 3 weeks of abstinence ($F = 16.9$, df 20,306, $P < 0.001$).

Positive correlations between the self-completed AWQ and interviewer-administered ASSA ($r = 0.60$, $P < 0.01$) indicated good agreement between these two scales, as did correlations between the observer-rated CGI and AWQ ($r = 0.55$, $P < 0.01$) and ASSA ($r = 0.64$, $P < 0.01$).

Amphetamine withdrawal: item scores

For in-patients undergoing methamphetamine withdrawal, all 10 AWQ items reduced significantly over the study period. Figure 2, panel 1 shows the pattern of AWQ items relating to increased sleep (mean = 1.38, SEM = 0.07), appetite (mean = 1.42, SEM = 0.07) and vivid, unpleasant dreams (mean = 0.36, SEM = 0.04). Figure 2, panel 2 shows the pattern of AWQ items relating to fatigue (mean = 0.62, SEM = 0.05), anhedonia (mean = 0.65, SEM = 0.05), motor retardation (mean = 0.48, SEM = 0.04) and dysphoria (mean = 0.60, SEM = 0.04). AWQ items: anxiety (mean = 0.53, SEM = 0.04), agitation (mean = 0.42, SEM = 0.04) and craving (mean = 0.35, SEM = 0.04) are shown in Fig. 2, panel 3.

Twelve of the 18 ASSA items reduced significantly over the first 3 weeks of abstinence. Figure 2, panel 4 shows the pattern of six of the ASSA items that changed: symptoms of inactivity (mean = 1.02, SEM = 0.11), fatigue (mean = 0.56, SEM = 0.08), craving frequency (mean = 0.58, SEM = 0.04), craving intensity (mean = 0.60, SEM = 0.07), hypersomnia (mean = 0.74, SEM = 0.10) and craving for carbohydrates (mean = 1.69, SEM = 0.10).

Figure 2, panel 5 shows a further six of the ASSA items that showed significant change, including anhedonia (mean = 0.55, SEM = 0.08), tension (mean = 0.47, SEM = 0.06), poor concentration (mean = 0.35, SEM = 0.04), bradycardia (mean = 0.99, SEM = 0.07), hyposomnia (mean = 0.43, SEM = 0.07) and depression (mean = 0.39, SEM = 0.06). Figure 2, panel 6 shows the six ASSA items that did not change significantly. These included hyperphagia (mean = 1.11, SEM = 0.10), hypophagia (mean = 0.14, SEM = 0.04), irritability (mean = 0.40, SEM = 0.06), anxiety (mean = 0.46, SEM = 0.08), paranoid ideation (mean = 0.02, SEM = 0.01) and suicidal ideation (mean = 0.35, SEM = 0.04).

Predictors of withdrawal severity

Using the total AWQ score as the dependent variable, linear regression analysis was performed to identify predictors of withdrawal severity during the first 3 weeks of abstinence. Using the standard method, three continuous variables were entered into the regression model: age, length of methamphetamine use and number of DSM-IV amphetamine dependence criteria met. Although the model was significant ($F = 29$, df 3,346, $P < 0.001$), only 21% of the variance in withdrawal scores was predicted. Multi-collinearity was satisfactory: the highest correlation between independent variables was $r = 0.27$ between age and DSM-IV criteria. All three independent variables were significant positive predictors of withdrawal severity: years of age ($\beta = 0.33$, $P < 0.001$), years of methamphetamine use ($\beta = 0.27$, $P < 0.001$) and number of DSM-IV amphetamine dependence criteria met ($\beta = 0.11$, $P = 0.03$).

Radial pulse and blood pressure did not change significantly, staying within normal limits for the duration of the study. However, when pulse rate was changed from a continuous to a categorical variable for the ASSA scale item 'bradycardia', a significant change was revealed (see Fig. 2, panel 5).

Sleep

For in-patient participants, total hours of sleep (over the 24-hour period) changed significantly over the study period, peaking on the fifth day of abstinence ($F = 3.12$, df 20,310, $P < 0.001$, Fig. 3: panel 1). For the comparison group, total hours of sleep (mean = 7.4, SEM = 0.14, Fig. 3: panel 2) fell within the range for normal healthy adults [33], as did the sleep onset latency in minutes (mean = 20.0, SEM = 0.4, Fig. 3: panel 3) [34].

Similarly, all the in-patients' other sleep-related variables, including hours of daytime sleep ($F = 3.21$, df 20,310, $P < 0.001$, Fig. 3: panel 1), hours of night-time sleep ($F = 1.85$, df 20,310, $P = 0.015$, Fig. 3: panel 1), sleep latency ($F = 1.88$, df 20,306, $P = 0.014$, Fig. 3: panel 3), number of awakenings during the night ($F = 2.39$, df 20,309, $P < 0.001$, Fig. 3: panel 4), quality of sleep ($F = 2.11$, df 20,310, $P = 0.004$, Fig. 3: panel 5), clearheadedness on awakening ($F = 3.40$, df 20,309, $P < 0.001$, Fig. 3: panel 6), satisfaction with sleep

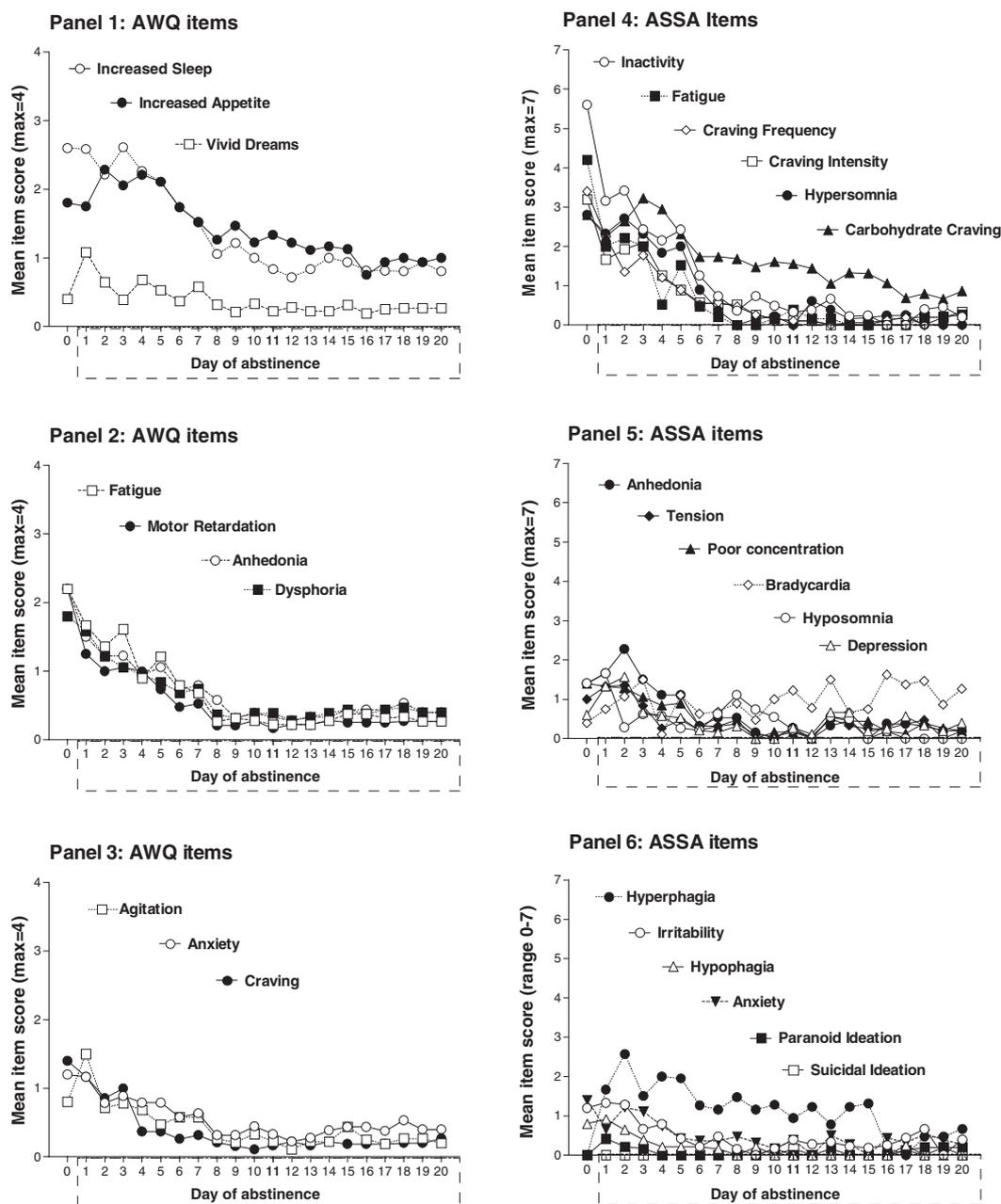**Figure 2** Distribution of item scores

($F = 1.92$, df 20,310, $P < 0.01$, Fig. 3: panel 7) and depth of sleep ($F = 1.70$, df 20,310, $P = 0.032$, Fig. 3: panel 8) changed significantly. All sleep variables were significantly different to the comparison group with the exception of satisfaction with sleep.

Predictors of sleep patterns during withdrawal

Using the total hours of sleep during each 24-hour period as the dependent variable, linear regression analysis was performed to identify predictors of sleep patterns during the first three weeks of abstinence. Three continuous

variables were entered into the regression model using the standard method: methamphetamine cost per day during the month prior to admission, years of regular methamphetamine use and number of DSM-IV amphetamine dependence criteria met. While the model was significant ($F = 8.4$, df 3,346 $P < 0.001$), only 26% of the variance in hours of sleep was predicted. Multicollinearity was satisfactory: the highest correlation between independent variables was $r = 0.4$ between methamphetamine cost per day and DSM-IV criteria. Two independent variables were significant positive predictors of sleep: methamphetamine cost ($\beta = 0.23$,
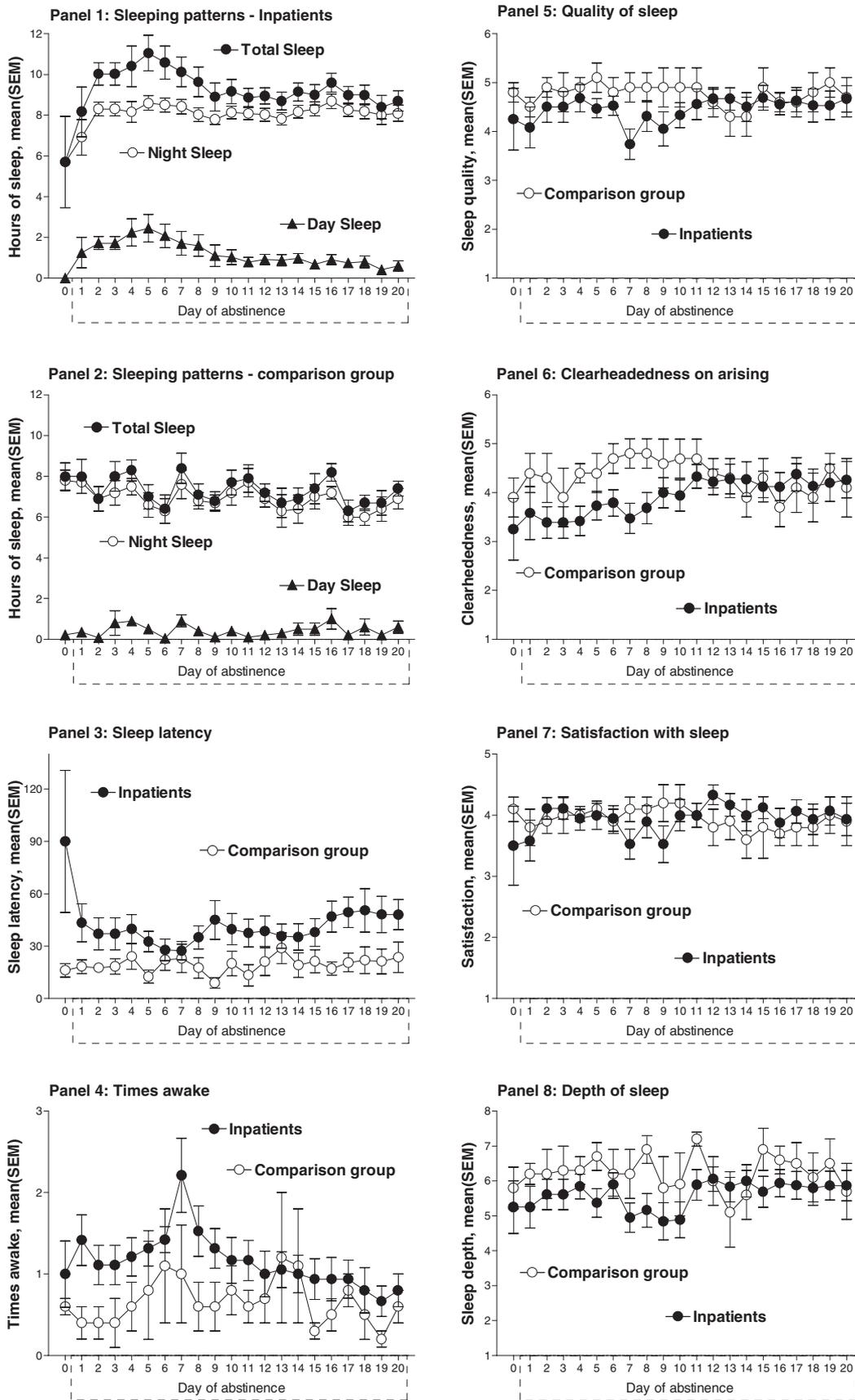
Figure 3 Sleep patterns

$P < 0.001$) and years of use ($\beta = 0.11$, $P = 0.025$), while the number of DSM-IV criteria was negatively related to total hours of sleep during withdrawal ($\beta = -0.16$, $P = 0.004$).

Depression

On average, admission BDI scores fell into the moderate category (mean = 23.6, SEM = 2.2). At the beginning of weeks 2 (mean = 12.1, SEM = 3.0) and 3 of in-patient treatment (mean = 9.8, SEM = 3.0), BDI scores had reduced on average to the minimal depression category. This reduction in BDI scores over the first 3 weeks of abstinence was significant ($F = 7.6$, df 2,54, $P < 0.01$). On admission, 14% of patients each fell into the minimal and mild depression categories while 48% and 24% fell into the moderate and severe categories, respectively. By the beginning of the third week of abstinence, almost two-thirds (65%) had minimal depression while 12% each fell into the mild, moderate and severe BDI depression categories.

DISCUSSION

In this study, we quantified the natural history of methamphetamine withdrawal during the first 3 weeks of abstinence. Overall symptom severity as measured by self-report, interviewer-administered and observer-rated instruments declined from a high initial peak within 24 hours of the last use of amphetamines, reducing to near comparison group levels by about the end of the first week of abstinence. Two phases were identified: an acute phase that occurred during the first week, and a subacute phase lasting for at least 2 further weeks. Withdrawal severity was greater in those in-patients who were older, more dependent and who had been using methamphetamine longer.

The methamphetamine withdrawal syndrome was characterized principally by increases in sleeping and appetite. A cluster of depression-related symptoms including inactivity, fatigue, anhedonia and dysphoria were marked during the first week, but had largely resolved by the end of the acute phase of abstinence. Less severe symptoms of withdrawal included anxiety, motor retardation, agitation, vivid dreams, craving, poor concentration, irritability and tension. Of the withdrawal symptoms measured, most had reduced towards comparison group levels by the end of the first week of abstinence. Exceptions included the sleep and appetite-related symptoms that persisted through weeks 2 and 3 of abstinence (the subacute phase). The relative increase in bradycardia during weeks 2 and 3 possibly reflected a rebound phenomenon in cardiac function following cessation of acute withdrawal. Levels of paranoid and suicidal ideation remained low throughout the first 3 weeks of abstinence.

Our results supported clinical reports of a 'crash' period characterized by relative oversleeping during the first week of abstinence. The increase in total hours of sleep between pre-admission and the peak at day 5 when participants slept for around 11 hours was striking. However, there was no insomnia following the 'crash'. Instead, hours of sleep gradually declined from their peak until the ninth day, after which total hours of sleep remained stable at around 9 hours for the rest of the monitoring period. However, the quality and depth of sleep in patients undergoing withdrawal treatment decreased at the end of the acute phase and did not return to previous levels until the third week of abstinence. Therefore, while in-patients had a greater total amount of sleep, in contrast to the comparison group their sleep patterns were of a poorer quality as they took significantly longer to fall asleep and had a greater number of awakenings during the night. Additionally, clearheadedness on arising did not reach comparison group levels until about the middle of the second week of abstinence.

Our findings contrast with an earlier investigation into sleep duration in hospitalized amphetamine users in the United Kingdom [23]. In this study, Gossop and colleagues found that in comparison to controls, the number of hours of night-time sleep was significantly less in the amphetamine users over the 20-day study period. While hours of sleep for amphetamine users were greater than or similar to controls on nights 1–5 of admission, amphetamine users slept less than controls on nights 6–20 when the UK study ended. These authors suggested that withdrawal insomnia may be dose-related. Our finding that the cost of methamphetamine used in the month prior to admission and the length of regular use were significant positive predictors of sleep during withdrawal supported this contention.

The modified CSSA [27] showed satisfactory reliability when used to measure methamphetamine withdrawal and was significantly related to the established scale, the AWQ [24]. Importantly, the modified CSSA provided useful information on additional symptoms of amphetamine withdrawal, particularly items measuring concentration, tension and inactivity. Future studies should investigate the psychometric properties of this scale in a larger sample of amphetamine users.

Unlike alcohol [35] or opioid withdrawal [36], there were no directly measurable amphetamine withdrawal signs as objective measures such as pulse and blood pressure remained within normal limits for the duration of the study period. However, the moderately strong relationship between subjective withdrawal symptoms and the observer-rated evaluation of withdrawal severity indi-

cated that experienced clinicians are able to provide a reasonably accurate and consistent judgement as to the current level of discomfort experienced by patients in amphetamine withdrawal. Additionally, the number of hours of sleep provides an observable indication of the time course and severity of withdrawal.

Although the in-patient participants in this study were moderately depressed on admission for treatment, depression had resolved after one week of abstinence. These findings do not support previous studies showing prolonged depression following cessation of dependent amphetamine use [12,22].

CONCLUSION

This study has provided evidence of a methamphetamine withdrawal syndrome that can be categorized into two phases: an acute phase lasting 7–10 days following cessation of dependent use during which overall symptom severity declined in a linear pattern from a high initial peak. This was followed by a subacute phase lasting at least 2 weeks following the end of the acute phase during which most withdrawal symptoms remained relatively mild and stable. During the acute phase, in-patients had increased sleeping and eating, depression-related symptoms and, less severely, anxiety and craving-related symptoms. Oversleeping was marked during the acute phase and despite a reduction in sleep quality, was not followed by a period of insomnia during the subacute phase. Older, more dependent patients who had been using methamphetamine longer had a more severe withdrawal course.

Acknowledgements

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