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Psychological treatments for stimulant misuse, comparing and contrasting those for amphetamine dependence and those for cocaine dependence

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Abstract

Purpose of review—The aim is to compare and contrast psychological treatments for amphetamine and cocaine dependence.

Recent findings—Stimulant dependence, in the form of cocaine or amphetamine/methamphetamine dependence, is prevalent worldwide, and their ratio may vary across different countries and regions of countries. The treatment of stimulant disorders has greatly advanced in recent years, and scientific evaluation of behavioral therapies, using randomized clinical trials designs and a stage-wise approach, have demonstrated the safety and efficacy of interventions. Psychological interventions such as cognitive behavioral therapy and contingency management for cocaine and methamphetamines use disorders are well tolerated and moderately effective in achieving drug abstinence. There is evidence that contingency management interventions can help to improve retention in treatment and, in turn, other treatment outcomes. Although there are important differences in the neuropsychiatric and medical consequences of cocaine and amphetamine use disorders, there is currently no evidence for a differential treatment effect of any psychosocial treatment in the management of these disorders.

Summary—As there are no Food and Drug Administration-approved medications for the treatment of these disorders, psychological interventions form the basis of their treatment. More research is needed to address the specific psychosocial needs of cocaine and amphetamine-dependent individuals in order to improve their treatment outcomes.

Keywords

amphetamine; behavioral; cocaine; methamphetamine; treatment

Introduction

According to the United Nations Office on Drug Use and Crime, there are 24.9 million amphetamine and 16 million cocaine users in the world [1•]. Cocaine and amphetamine/methamphetamine use disorders have regional patterns. For example, amphetamine/methamphetamine abusers and cocaine abusers in Australia and New Zealand constitute 17 and 0.4%, respectively, of the 94 293 persons treated in Oceania, whereas in Africa

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amphetamine users and cocaine users constitute 5 and 9.6%, respectively, of the 34 187 people treated for substance abuse disorders. In the United States, according to the National Household Survey on Drug Use and Health of 2006 [2], among persons aged 12 years or older, the past-month prevalence of cocaine use was 2.4% and stimulant use (including amphetamine and methamphetamine) was 1.2%. The same survey shows regional differences in the frequency of cocaine and stimulant use. For example, the past-year prevalence of methamphetamine use in the northeast region was 0.3%, whereas in the west coast region it was 1.6%. Furthermore, there is a high demand for treatment of these disorders. It has been reported that, in 2006, approximately 1.5 million people received treatment for cocaine abuse or dependence, and nearly 400 000 received treatment for stimulant abuse or dependence. Currently, there are no approved medications for the treatment of cocaine and/or amphetamine/methamphetamine dependence, and behavioral and psychological treatments form the basis of treatment for these stimulant disorders. This review will compare and contrast recent findings in the behavioral and psychological treatment of cocaine and amphetamine/methamphetamine use disorders.

Treatment of cocaine dependence

The development and testing of behavioral and psychosocial treatments for substance use disorders has been a priority of the National Institute on Drug Abuse (NIDA) for over 20 years [3]. A recent meta-analysis of psychosocial interventions, many funded by NIDA, evaluated treatments for cannabis, cocaine, opiate, and polysubstance abuse that were published through 2005. For the analysis of cocaine treatments, nine studies of different psychosocial interventions were each compared with a control group [4••]. The interventions were contingency management (n = 4 studies), relapse prevention (n = 2 studies), cognitive behavioral therapy (CBT) (n = 1 study), CBT/group drug counseling (GDC) (n = 1 study), and CBT/contingency management (n = 1 study). Contingency management in this context is defined as positive reinforcement of desirable behaviors, usually drug-free urines, in individuals undergoing substance abuse treatment. The combined effect of the psychosocial treatments yielded a moderate-to-large Cohen's effect size [d = 0.62, 95% confidence interval (CI) 0.16–1.08]. Abstinence rates for the cocaine users averaged 31.7%, although the definition of significant abstinence varied across studies. Placebo abstinence rates for the cocaine group alone were not reported, although a combined abstinence rate of 13% was reported for all control groups across all drug conditions. The authors noted that the effect sizes for psychosocial treatments across all drug treatment groups were comparable with those seen with pharmacotherapy for anxiety disorders.

With regards to contingency management, a meta-analysis of 12 studies of voucher-based contingency management for the treatment of cocaine dependence reported an average effect size r of 0.35, a moderate effect size [5••]. So far, of all the behavioral therapies, contingency management has shown the highest efficacy for the treatment of cocaine addiction.

Psychosocial interventions are usually offered in the clinical trials testing medications for stimulant addiction, and the outcome of the interventions may be affected by sociodemographic factors. For example, NIDA funded a series of clinical trials known as the Cocaine Rapid Efficacy Screening Trial (CREST) in which 18 medications were assessed for efficacy against a common placebo at five clinical sites [6]. The psychosocial treatment in all studies was a relapse prevention treatment manual based on models of CBT [7]. This psychosocial therapy was selected due to an expectation that it would enhance retention in the trials. Abstinence was defined using a composite measure of urine benzoylecgonine and self-report. A pooled analysis of 345 individuals (88% crack cocaine users) across all trials showed that there were no significant medication effects when the medications were collapsed across the following four groups: antidepressants, dopamine agonists, mood stabilizers, and nootropics/neuroprotectives [8].

In the latter study, approximately 60% of the individuals were retained in the drug and placebo groups during the trial, although 70% of the individuals were retained until the last week of the study. Two-week abstinence rates averaged 13.7% across all individuals. Subgroup analyses were performed. Three subgroups had better 2-week abstinence rates than the grand average: two of eight women with at most 5 years of prior use and at least 40 years of age, 10 of 33 non-African–American men with at least four cocaine-positive urines during the baseline period and more than 4 years of cocaine use, and 16 of 38 men with at most three cocaine-positive urines and less than 20 years of cocaine use. Abstinence rates below the average were seen in the following groups: two of 76 women with at least 5 years of prior use, zero of 13 women with at most 5 years of prior use and younger than 40 years, African–American men with at least four cocaine-positive urines during the baseline period and at least 21 years of prior use, non-African–American men with at least four cocaine-positive urines and at most 4 years of prior use, and men with at most three cocaine-positive urines at baseline and at least 20 years of prior use. These data suggest that abstinence rates in clinical trials of interventions for cocaine dependence may vary as a function of the demographic composition of the trial participants.

Recent treatment research: psychosocial interventions

The majority of recent publications of psychosocial interventions for the treatment of cocaine dependence are evaluations of the effect of contingency management in a variety of settings, and sometime they have treatment objectives other than cocaine abstinence. One exception to this trend was a determination of whether a brief addition of motivational enhancement therapy (MET) to CBT would result in better outcomes [9]. Seventy-four cocaine users were randomized to either the CBT or CBT as well as MET group. Although cocaine users in the MET as well as CBT group had a greater commitment to abstinence, attended more sessions, and expected greater treatment success, there were no differences between the two groups.

An important international replication of the community reinforcement approach (CRA) as well as vouchers was reported by a Spanish treatment research group [10•]. In this study, 43 cocaine-dependent cocaine users (of whom 41 used the intranasal route) were randomized to CRA as well as vouchers or standard care. Twenty-four-week retention for the CRA as well as vouchers group (73%) was significantly better than that in the control group (43%, $P = 0.02$). Similarly, the 24-week abstinence rate in the CRA as well as voucher group (40%) exceeded that of the control group (21%, $P = 0.08$). Average duration of continuous abstinence was 4.35 months in the CRA as well as vouchers group versus 3.01 months for the control group ($P = 0.05$). The results suggest that the CRA as well as vouchers approach for treatment of cocaine dependence has generalizability outside the United States. There are two possible explanations for the differences seen in response in this study versus the CREST studies: the behavioral therapy of CRA as well as vouchers is possibly more potent than the relapse prevention therapy in the CREST trials, and the route of administration differences may signal a higher degree of dependence and relative lack of treatment responsiveness in the CREST studies, that is, predominantly crack users in CREST versus intranasal users in the Spanish study. Nonetheless, the treatment response seen in the CRA as well as vouchers group is impressive in terms of the percentage of responders and the length of abstinence.

A direct comparison study [11] of contingency management versus CBT was performed in 177 stimulant-dependent individuals ($n = 160$ cocaine users and 17 methamphetamine users). Participants were randomized to 16 weeks of contingency management, CBT, or contingency management as well as CBT. Contingency management produced better retention and less stimulant use during the treatment period. Three-week continuous abstinence percentages in the CBT, contingency management, and contingency management as well as CBT groups were 34.5, 60, and 69.5%, respectively. The contingency management and CBT as well as

contingency management groups were statistically significantly different from the CBT group ($P < 0.0001$) but not from each other. There was no additive effect of combining the therapies. The 17, 26, and 52-week follow-up urines did not show a difference across any of the groups. Contingency management may be a more effective treatment during therapy, but CBT appears equally effective in the postdischarge period. This suggests that either the effect of the contingencies can be short-lived when they are stopped or the effect of CBT persists during follow-up. A delay in the efficacy of CBT has been previously noted in cocaine users [12].

The addition of contingency management to standard treatment was evaluated in three separate trials comprising 387 cocaine users who were randomized to 12 weeks of standard care or standard care as well as contingency management [13]. Individuals in the standard care as well as contingency management groups achieved a greater degree of abstinence and a higher quality of life as scored on the Quality of Life Inventory.

Contingency management techniques have been applied to multiple situations involving cocaine users. A meta-analysis of day treatment and contingency management research studies in 644 homeless crack cocaine users reported that contingency management produced a 73% abstinence prevalence at the 2-month treatment point compared with 45% abstinence in a day treatment group and 12% abstinence for a no treatment group [14]. A study [15•] of homeless cocaine and alcohol users seeking shelter was conducted. Thirty participants were randomized to a contingency for maintaining abstinence from cocaine and alcohol or assessment only. All individuals in the contingency group completed the study. The contingent group also reported significantly fewer cocaine use days ($P = 0.020$) and fewer days of alcohol use ($P = 0.010$) than the assessment only group. A third study compared the effects of contingency management versus standard treatment in a group of 393 drug users (336 of whom were cocaine users) assessed for psychiatric symptom severity in a report that aggregated data across three studies [16]. All individuals were evaluated for addiction and psychiatric illness. Psychiatric severity was assessed using the addiction severity index, the brief symptom inventory, and the structured clinical interview for the diagnostic and statistical manual of mental disorders (DSM-IV). Individuals with moderate or high psychiatric severity tended to drop out at a higher rate than those assigned to the contingency management group ($P = 0.05$). The achievement of 8 weeks of continuous abstinence clearly favored the contingency management group ($P < 0.001$) but did not differ by psychiatric severity with the contingency management group.

Contingency management has also been evaluated in cocaine users outside of a treatment setting, that is, employment-based abstinence [17]. Fifty-six cocaine users were randomized to an abstinence and work group, whereas the others were assigned to a work only group. Participants could earn up to $40 in vouchers each workday, but the abstinence as well as work group had to provide cocaine-free urine samples to be able to work. The abstinence as well as work group submitted 29% cocaine-free urines compared with the 10% cocaine-free urines submitted by the work group ($P = 0.004$).

Contingency management has been reported to be enhanced by pharmacotherapy. Desipramine [18], bupropion [19], and citalopram [20] and flouxetine [21] have been shown to improve the number of cocaine-free urines in treatment studies when combined with contingency management. More research is needed to substantiate the effects of these antidepressants when used in conjunction with contingency management, especially in individuals who do not initially respond to contingency management [22•].

Treatment of amphetamine/methamphetamine dependence

Psychosocial interventions (cognitive therapy, CBT, and contingency management) used in the treatment of amphatemaine/methamphetamine dependence have been recently reviewed [23••]. Some of the noteworthy trials will be highlighted.

A large, multicenter trial compared the Matrix model, an empirically derived manualized 16-week therapy (with elements of CBT), with treatment as usual (TAU) in 978 methamphetamine-dependent individuals [24]. At most sites, the Matrix therapy was superior to TAU in terms of retention, session attendance, methamphetamine-free urines, and periods of continuous methamphetamine abstinence. However, individuals in the composite TAU group had equivalent reductions in methamphetamine use at discharge and the 6-month follow-up point. Individuals in the Matrix group were 27% more likely to complete treatment. Thus, the Matrix therapy's statistical superiority in retaining individuals ($P = 0.031$) may translate to a greater treatment efficiency over the TAU groups.

A brief (two or four session) CBT as well as a self-help booklet was compared with the efficacy of the self-help booklet in 214 regular amphetamine users randomized to one of the three conditions [25]. Compared with the control group, individuals randomized to the two CBT groups had significantly greater likelihood of being abstinent at the 6-month follow-up: 17.6% abstinence for controls, 33.8% abstinence for the two-session group ($P < 0.01$), and 37.9% abstinent for the four-session group ($P < 0.01$). The magnitude of the difference between the self-help group and the brief therapy groups is impressive. The investigators recommended a randomized control trial of a stepped-care model as a follow-on study.

The effects of 12 weeks of Matrix therapy compared with Matrix therapy as well as contingency management were assessed in 113 methamphetamine users (who met criteria for DSM-IV methamphetamine abuse or dependence) randomized to the two treatment conditions [26]. There were no differences in retention or the number of sessions attended across the two groups. The Matrix as well as contingency management group had significantly more methamphetamine-free urine samples ($P = 0.01$) and a greater mean period of continuous abstinence (4.6 versus 2.8 weeks, $P = 0.02$), demonstrating a clear treatment effect of an add-on contingency management. Moreover, abstinence during the last 4 weeks of the trial, irrespective of treatment assignment, increased the likelihood of a methamphetamine-free urine at the 3-month follow-up ($P = 0.01$) and at the 6-month follow-up ($P = 0.060$). Thus, abstinence at the end of the trial predicted abstinence at follow-up.

Contingency management has been assessed for its ability to reduce methamphetamine use and HIV risk behaviors in gay and bisexual men (GBM) [27]. In this study, 162 GBM were randomized to one of the four treatment assignments: CBT, contingency management, CBT as well as contingency management, and a culturally tailored CBT [group cognitive behavioral therapy (GCBT)]. Retention, methamphetamine use, and sexual risk behaviors were assessed. The contingency management group received an escalating reward value of vouchers for continuous methamphetamine-free urines with a reset to zero for use. The following significant differences were noted: retention ($P < 0.02$) and duration of continuous abstinence ($P < 0.001$) favored the contingency management and contingency management as well as CBT groups; and GCBT reduced the incidence of receptive unprotected anal intercourse during the first 4 weeks of treatment ($P = 0.01$). As methamphetamine use in this population is tied to HIV risk behaviors, the investigators commented that treatment merits considerations as an HIV prevention strategy.

Is there a differential treatment effect of psychosocial treatment in cocaine and methamphetamine users?

Given that methamphetamine users can present for treatment with greater medical and psychiatric disorders [28], the question has been posed as to whether there is a differential treatment effect for methamphetamine and cocaine users.

The initial study [29] of patients treated in the Matrix model that compared 500 methamphetamine users and 224 cocaine users found no differences in treatment efficacy across the two groups. A similar finding was reported by Copeland and Sorensen [30]. These investigators compared treatment response in 83 methamphetamine users and 262 cocaine users who attended an outpatient stimulant dependence treatment clinic. No differences were seen in the days of treatment, the number of group and individual sessions attended, the number of drug-free toxicology screens, and completion of treatment. Treatment outcomes of methamphetamine users compared with other drug users in the publicly funded treatment system in Washington State was recently reported [31]. Treatment completion, readmission to treatment, employment, and criminal justice involvement were tracked for 1 year following discharge. There were no differences in the treatment outcomes of interest when the outcomes of 2872 methamphetamine users were compared with those of 2399 ‘hard drug’ (cocaine, heroin, and other opiate) users. Many recent clinical trials have combined cocaine and methamphetamine users and analyzed the treatment effects in the combined stimulant user groups [31–33].

Conclusion

Psychosocial and behavioral treatments, notably CBT and contingency management, of cocaine and methamphetamines users are moderately effective. Adding contingency management to standard treatment can boost the treatment response. There is some evidence that contingency management can provide better retention even if no differences in treatment response are seen. This suggests that contingency management can increase treatment efficiency.

There is currently no evidence for a differential treatment effect of any psychosocial treatment in the management of cocaine and methamphetamine users in treatment, despite the worse medical and psychiatric condition of methamphetamine users.

The efficacy of psychological and behavioral treatments may be improved by using a chronic disease approach and, as such, providing treatments for a longer time and developing efficacious relapse prevention strategies. In addition, although drug use abstinence may be the ultimate goal of treatment, psychological and behavioral interventions aimed at reducing drug use and/or preventing the medical and psychosocial consequences of drug abuse should be investigated.

Pharmacotherapy can enhance the effect of contingency management to increase abstinence from cocaine. More research is needed to confirm these initial findings and extend them to treatment of methamphetamine users.

Acknowledgments

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 333).

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