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Randomized, placebo-controlled trial of sertraline and contingency management for the treatment of methamphetamine dependence

Steven Shoptaw [a,*], Alice Huber [b], James Peck [b], Xiaowei Yang [c], Juanmei Liu [d], Jeff Dang [a], John Roll [e], Benjamin Shapiro [f], Erin Rotheram-Fuller [a], Walter Ling [b]

[a] *Center for Health Promotion and Disease Prevention, Department of Family Medicine, David Geffen School of Medicine at UCLA, 10880 Wilshire Blvd, Suite 1800, Los Angeles, CA 90024, United States*
[b] *Integrated Substance Abuse Programs, Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine at UCLA, 11075 Santa Monica Blvd, Suite 200, Los Angeles, CA 90025, United States*
[c] *Department of Public Health Sciences One Shields Avenue, TB-168, University of California, Davis, CA 95616-8638, United States*
[d] *Department of Psychology-Measurement, UCLA, Box 951563, 1285 FH, Los Angeles, CA 90095-1563, United States*
[e] *WSU-Spokane Health Sciences, Washington State University, P.O. Box 1495, Spokane, WA 99210-1495, United States*
[f] *Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA, 760 Westwood Plaza, C-8 mailroom, Los Angeles, CA 90024, United States*

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Abstract

Background: Methamphetamine dependence and associated medical and psychiatric concerns are significant public health issues. This project evaluated the efficacy of sertraline (50 mg bid) and contingency management (CM) for the treatment of methamphetamine dependence.
Method: In this randomized, placebo-controlled, double-blind trial, participants completed a 2-week non-medication baseline and were randomized to one of four conditions for 12 weeks: sertraline plus CM ($n = 61$), sertraline-only ($n = 59$), matching placebo plus CM ($n = 54$), or matching placebo-only ($n = 55$). All participants attended clinic thrice-weekly for data collection, medication dispensing, and relapse prevention groups. Outcomes included methamphetamine use (urine drug screening and self-reported days of use), retention (length of stay), drug craving (visual analogue scale), and mood symptoms (Beck Depression Inventory).
Results: No statistically significant main or interaction effects for sertraline or CM in reducing methamphetamine use were observed using a generalized estimating equation (GEE), although post hoc analyses showed the sertraline-only condition had significantly poorer retention than other conditions (χ^2 (3) = 8.40, $p < 0.05$). Sertraline conditions produced significantly more adverse events than placebo conditions. A significantly higher proportion of participants in CM conditions achieved three consecutive weeks of methamphetamine abstinence than those in non-CM conditions.
Conclusions: These data do not demonstrate improved outcomes for sertraline versus placebo for treatment of methamphetamine dependence; indeed, they suggest sertraline is contraindicated for methamphetamine dependence. Findings provide support for the use of contingency management for treatment of methamphetamine dependence.

Keywords: Methamphetamine; Sertraline; Contingency management; Drug abuse; Medications

1. Introduction

The proliferation of methamphetamine dependence, and its serious consequences to medical, public health, law enforcement, and criminal justice systems in broad sections of the United States, has engendered an urgent need for effective interventions. Treatment admissions for methamphetamine dependence now outpace those for cocaine or heroin dependence in broad sections of the country (CESAR, 2005). In addition to the numerous criminal justice (Hser et al., 2004; Cretzmeyer et al., 2003), medical, and psychiatric sequela (Peck et al., 2005a) of methamphetamine dependence, it is strongly associated with HIV and other infectious diseases among men who have sex with men (Shoptaw et al., 2005; Patterson et al., 2005), and increasingly among populations historically considered at lower risk for HIV (CDC, 2004).

* Corresponding author. Tel.: +1 310 312 794 0619; fax: +1 310 312 0552.
E-mail address: sshoptaw@mednet.ucla.edu (S. Shoptaw).

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Methamphetamine withdrawal symptoms, including fatigue, anhedonia, depressed mood, and hypersomnia, are common to depression and are often severe enough to precipitate relapse (Peck et al., 2005b). Methamphetamine produces neurotoxic effects in monoaminergic neurons and related neural structures also associated with depression (Guilarte et al., 2003). Early work demonstrating that lesions or neurotoxins that inhibit 5-HT signaling caused animals to consistently self-administer more amphetamine (Leccese and Lyness, 1984; Lyness et al., 1980) suggested potential usefulness of 5-HT reuptake inhibitors in decreasing the reinforcing effects of methamphetamine and associated neurotoxicity. This strategy has been implemented in trials of the selective serotonin reuptake inhibitors (SSRIs) fluoxetine (Batki et al., 1999) and paroxetine (Piasecki et al., 2003), both of which have shown no efficacy for reducing methamphetamine use.

Although efforts to develop an effective pharmacotherapy for methamphetamine dependence have been unsuccessful, behavioral and cognitive behavioral therapies have shown efficacy for reducing stimulant use (Carroll et al., 2004; Rawson et al., 2004) and the depressive symptoms associated with methamphetamine use (Peck et al., 2005b). Contingency management (CM) is an application of operant conditioning that manipulates available reinforcers to shape behavior. There is substantial evidence to support its use for treatment of dependence on alcohol and numerous drugs including heroin, cocaine, and marijuana, for improving treatment-related outcomes (see Carroll and Onken, 2005 for review), and more recently with methamphetamine-dependent individuals (Shoptaw et al., 2005). The Matrix Model is an integrative psychosocial intervention that blends elements of motivational interviewing, family education, relapse prevention, and psychoeducational skills training. Matrix Model treatment outperformed standard treatments in a multi-site clinical trial of interventions for methamphetamine dependence (Rawson et al., 2004) and the model has been used as a psychosocial platform in clinical trials of medications for stimulant dependence (Shoptaw et al., 2003).

This study conducted a randomized placebo-controlled trial of sertraline, a potent SSRI with a strong safety profile, and of contingency management for methamphetamine dependence using a counseling platform of Matrix Model relapse prevention groups. The primary outcomes were defined a priori as methamphetamine use and retention in treatment. Secondary outcomes included craving for methamphetamine, depression, and adherence to study medication. It was predicted that participants assigned to receive sertraline would achieve significantly greater reductions in methamphetamine use and significantly longer retention in treatment than participants assigned to receive placebo, and that this effect would be optimized using contingency management. It was also predicted that participants assigned to receive sertraline would report significantly greater reductions in methamphetamine cravings and depressive symptoms, and would achieve significantly better adherence to study medication regimen than those assigned to receive placebo.

2. Method

2.1. Participants

The Friends Research Institute West Coast Institutional Review Board provided oversight of all procedures in accordance with the Belmont Report.

Participants were males and females (non-pregnant and non-lactating) between the ages of 18 and 65 who met criteria for methamphetamine abuse or dependence verified by the Structured Clinical Interview for the DSM-IV (SCID; Spitzer et al., 1995). Potential participants were excluded if they had a primary medical condition that might interfere with safe study participation, current pharmacotherapy for which concurrent treatment with a selective serotonin reuptake inhibitor would be contraindicated, a psychiatric condition identified by the SCID that required pharmacological or behavioral intervention, or SCID-diagnosed dependence on opioids, cocaine, alcohol, or benzodiazepines.

2.2. Measures

The Structured Clinical Inventory for the DSM-IV (SCID) was used to verify abuse or dependence on methamphetamine and to assess for psychiatric disorders or concurrent substance dependence that might require exclusion from the study.

Directly observed urine drug screening was used to verify methamphetamine use or abstinence. Assays were performed using SYVA EMIT. Each sample was tested for metabolites of methamphetamine. The first sample collected each study week was also tested for metabolites of opiates, cocaine, marijuana, and benzodiazepines. Results of these tests were used to enhance clinical care by alerting study staff to use of other drugs.

Retention was defined as the number of days from randomization to completion or early termination from the study. Participants were terminated from the study if they missed six consecutive scheduled clinic visits. Participants who reported unacceptable levels of side effects and wished to discontinue medication were terminated from the study but were give the option of continuing to attend the relapse prevention groups as a "treatment-only" participant for the full 12 weeks.

Depressive symptoms were assessed using the beck depression inventory (Beck, 1967), a 21-item self-report measure that was collected weekly.

Craving for methamphetamine was assessed using a 100 mm visual analogue scale asking participants to rate their most intense craving in the past 24 h from 0 (none at all) to 100 (the most intense imaginable).

To monitor medical safety, a complete physical examination, blood chemistry (including complete blood count with differential), urinalysis and 12-lead electrocardiogram were conducted at baseline and termination.

At each clinic visit, the study nurse utilized a structured questionnaire to query participants about side effects and other adverse events since the prior clinic visit. Adverse events for each participant were recorded and classified according to type, severity, and frequency.

Pill counts served as the primary marker of adherence to study medication regimen. Participants exchanged their medication bottle on the first clinic visit of each study week. At this visit, the research nurse counted and recorded the number of tablets remaining in the old bottle and recorded the number of tablets dispensed in the new bottle. For the purpose of data analysis, the number of tablets returned each week was subtracted from the number dispensed. This number was then divided by the number dispensed to obtain a percentage medication adherence variable. For those who terminated study participation early, only those tablets that were verified from returned medication bottles were included in the pill counts.

2.3. Medication dose

Sertraline (Zoloft®) and identical placebo were provided by the manufacturer (Pfizer Inc.) in 50 mg tablet doses. All participants were started on sertraline or placebo at 50 mg/day. On the eighth day following randomization, dose was increased to 50 mg bid and this dose was maintained for the duration of the trial. This dose was selected because it represented a mid-range effective dose (effective range 50–200 mg/day; see Zoloft® package insert) presumed by study investigators to result in fewer side effects than higher doses.

2.4. Contingency management procedures

Participants receiving contingency management provided observed urine samples on Mondays, Wednesdays, and Fridays. Samples that did not contain metabolites of methamphetamine qualified for a voucher that became increasingly valuable with continued abstinence. The voucher for the initial metabolite-free sample was worth US$ 2.50 and increased in value by US$ 1.25 for each consecutive metabolite-free sample. Each third consecutive metabolite-free sample earned a US$ 10.00 bonus voucher. Participants who produced a missing or methamphetamine-positive sample did not receive a voucher for that visit and the value of the next metabolite-free urine sample was set at US$ 2.50. A reset procedure was used following provision of a methamphetamine-positive sample such that after the subsequent third consecutive metabolite-free sample, the participant was returned to the place in the reinforcement schedule immediately prior to the missed or positive sample. All vouchers were redeemed for goods or services. No cash was provided.

2.5. General procedures

All study procedures took place at a Friends Research Institute clinical research site in Rancho Cucamonga, CA, a suburban area approximately 50 miles east of Los Angeles. Potential participants were recruited from the surrounding area using radio and print advertisements. Following provision of signed informed consent, potential participants began a 2-week, non-medication baseline during which information was collected to document inclusion and exclusion criteria.

To assist in initiating abstinence during the non-medication baseline, participants could attend twice-weekly early recovery skills groups. The topics for these four 60 min, early recovery skills groups included: Getting rid of paraphernalia; Scheduling; Introduction to 12-Step Groups; and HIV-risk reduction.

At the end of the 2-week baseline, participants who met all inclusion and no exclusion criteria were randomized to study condition. An urn randomization procedure (Stout et al., 1994) provided multivariate balance across gender, ethnicity, and years of education. Upon randomization, the research nurse observed the first dose of study medication.

A psychosocial platform of thrice-weekly 90 min Matrix Model relapse prevention groups was provided (Rawson et al., 2004). This evidence-based treatment draws upon principles of social learning theory, behavioral and cognitive behavioral therapies, and psychological and HIV-risk education to teach skills for initiating abstinence and preventing relapse. The model is standardized and manual-driven. The therapist held a masters degree and received training to proficiency in the model. Group sessions were audiotaped and approximately 15% were reviewed to assess fidelity to the model. Information from weekly supervision and audiotapes provided corrective feedback to the therapist and monitored participant safety.

2.6. Data analysis

Primary outcomes were methamphetamine use and treatment retention. Methamphetamine use was assessed by compiling urine drug screening results into aggregates: the treatment effectiveness score (TES; Ling et al., 1997) and the longest period of consecutive methamphetamine metabolite-free urine samples. The TES score is the average number for each treatment condition of drug metabolite-free urine samples (range = 0–36). The TES uses a denominator of the total possible urine samples – in this case, 36. Secondary outcomes were craving for methamphetamine (VAS), depressive symptoms (BDI), and medication adherence. Medication adherence was calculated as the percentage of participants per condition who achieved 80% or greater documented adherence. The type and incidence (unique adverse events reported for each participant) of adverse events was tabulated for the sertraline and placebo conditions and analyzed using Chi-square. Unique adverse events were also combined into the two broad categories of gastrointestinal effects and anticholinergic effects and were analyzed using Chi-square.

Data were systematically reviewed for entry errors and univariate normality (Tabachnick and Fidell, 1996). Univariate tests between the conditions along demographic, drug use, and mood variables were examined using Chi-square and analysis of variance (ANOVA) where appropriate. A Fisher's exact test was used for categorical data when the contingency table contained sparse cells (Wickens, 1998).

Prior to testing hypotheses, a limited set of demographic and drug use variables were compared between participants excluded from the medication trial and those who were randomized to condition to better characterize those randomized to the study. Project hypotheses for medication and behavioral therapy effects on methamphetamine use were tested using a generalized estimating equation (GEE; Zeger and Liang, 1986) and a random effects Markov transition model (REMTM) that maximized use of available data. The REMTM assumed a first order covariance structure where previous observations inform the probability of the next observation. This method has been used in other Phase II clinical trials (Shoptaw et al., 2003). Differences in retention by condition were evaluated using a Kaplan–Meier survival function (Allison, 1995). Measures of mood (BDI) and craving (VAS) were evaluated using a mixed model approach (Singer, 1998). A generalized linear model with a Poisson distribution for count data was used for the longitudinal analysis of pills taken during the study. All analyses were run in SPSS 12.0 (SPSS Inc., 2004) and SAS for Windows 9.0 (SAS Institute Inc., 2004).

3. Results

3.1. Sample characteristics

A total of 414 treatment-seeking individuals with methamphetamine abuse or dependence began screening procedures for this study (Fig. 1). Of these, 229 participants were randomized to study condition: sertraline plus CM ($n = 61$), sertraline-only ($n = 59$), placebo plus CM ($n = 54$), or placebo-only ($n = 55$). Participants not randomized to the trial reported heavier use of methamphetamine than those randomized to the study as measured by number of days of methamphetamine use in the 30 days prior to study entry ($M_{\text{non-rand}} = 22.0$ days (10.3), $M_{\text{rand}} = 13.0$ days (9.1); $t(397) = 9.33$, $p < 0.001$) and by amount of money spent on methamphetamine in the 30 days prior to study entry ($M_{\text{non-rand}} =$ US$ 436 (562), $M_{\text{rand}} =$ US$ 311 (450); $t(308) = 2.18$, $p = 0.03$). Baseline demographic and drug use variables across conditions are presented in Table 1. Although the study design specified that participants meeting criteria for abuse versus dependence would be balanced across study conditions, all but two of the randomized participants met criteria for dependence, making this procedure unnecessary.

3.2. Methamphetamine use outcomes

A modeling solution showed no statistically significant main effects for the sertraline or the contingency management conditions on methamphetamine use outcomes. Similarly, there was no statistically significant interaction. Post hoc evaluation of the effects of the four conditions on urine drug screening results showed that participants in the sertraline-only condition provided significantly more metabolite-positive urine samples compared to the other conditions over the trial (GEE model: χ^2 (1) = 5.02, $p < 0.05$; Fig. 2).

Significantly fewer participants assigned to the sertraline-only condition (25.4%) achieved the outcome criterion of at least 3 weeks of consecutive methamphetamine metabolite-free urine samples compared to the other conditions (sertraline plus contingency management = 42.6%, placebo plus contingency management = 51.9%, and placebo-only = 41.8%; χ^2 (3) = 8.6,

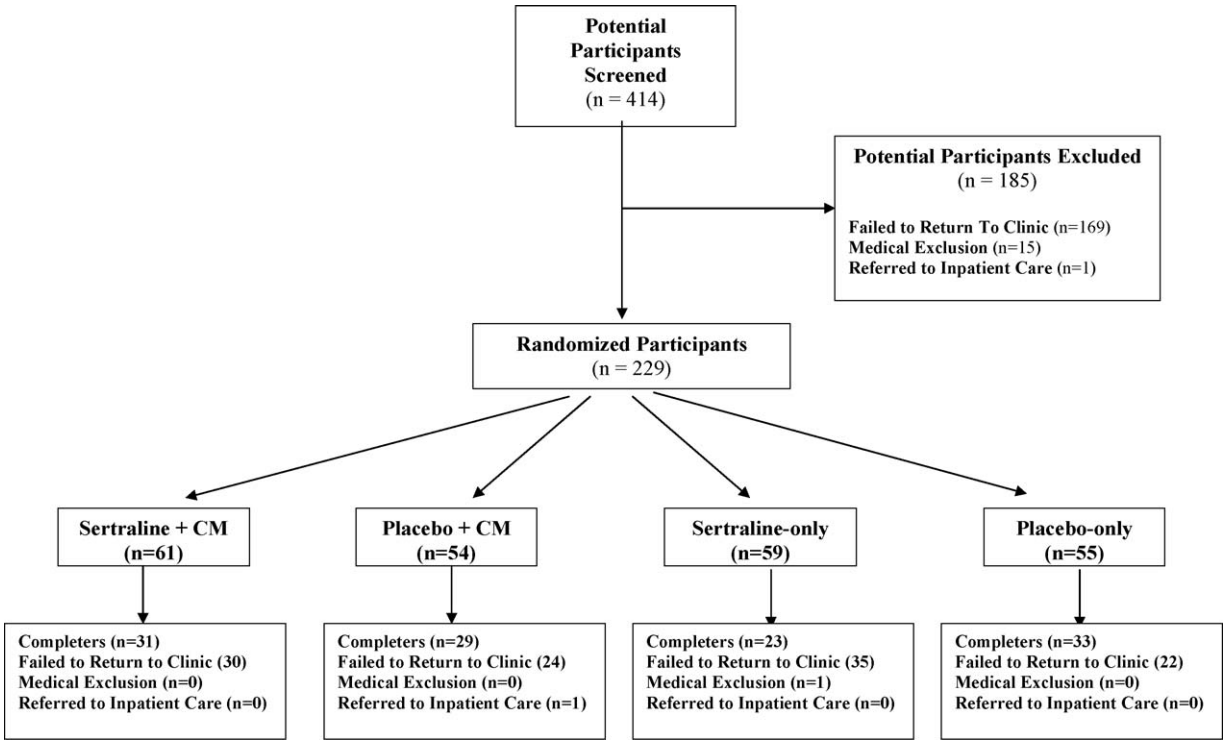

Fig. 1. Schematic of trial progress. Proportion of study completers vs. early terminators not statistically significantly different between study conditions.

Table 1
Baseline demographic, psychological status, and drug use variables by condition

	Sertraline + CM, $n = 61$, M ± S.D. or %	Placebo + CM, $n = 54$, M ± S.D. or %	Sertraline-only, $n = 59$, M ± S.D. or %	Placebo-only, $n = 55$, M ± S.D. or %
Age (in years)	34.1 (6.8)	31.3 (6.7)	33.5 (7.3)	33.3 (7.3)
Gender				
Male	60.7	64.2	61.4	60.4
Female	39.3	35.8	38.6	39.6
Ethnicity				
Caucasian	73.8	77.4	73.7	72.2
African American	1.6	0.0	0.0	0.0
Asian	1.6	1.9	1.8	1.9
Latino	23.0	20.7	24.5	25.9
Marital status				
Married	25.0	28.3	29.3	22.2
Never married	41.7	41.5	43.1	35.2
Divorced/separated	33.3	30.2	27.6	42.6
Education (in years)	12.1 (1.7)	12.0 (1.5)	12.2 (1.3)	11.9 (2.0)
Employment (past 30 days)				
Full time	60.7	50.9	52.6	51.9
Part time	18.0	13.2	24.6	16.7
Unemployed/student	21.3	35.9	22.8	31.4
Income in past 30 days (US$)	810 (1016)	812 (1693)	831 (1137)	638 (883)
Beck Depression Inventory	13.2 (8.7)	13.4 (6.9)	14.6 (9.6)	13.5 (8.8)
Days drank alcohol to intoxication (in past 30)	2.7 (5.9)	3.0 (6.1)	1.8 (4.4)	2.7 (6.3)
Days MA use (in past 30)	13.2 (9.2)	13.7 (8.8)	13.7 (9.0)	11.2 (9.4)
Years MA use	10.1 (6.0)	8.7 (5.4)	9.9 (6.1)	8.5 (4.8)

No differences significant at $p < 0.05$.

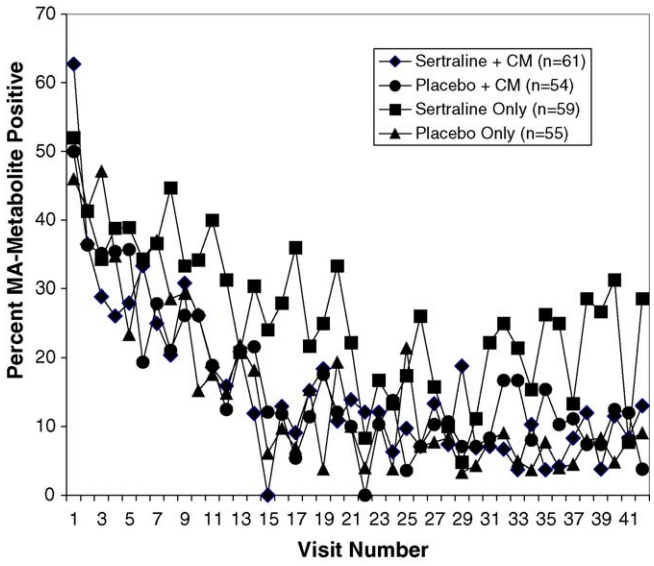

Fig. 2. GEE model of urinalysis results by treatment condition. Sertraline-only group provided more methamphetamine metabolite-positive urine samples than other study conditions (GEE analysis: χ^2 (1) = 5.02, $p < 0.05$).

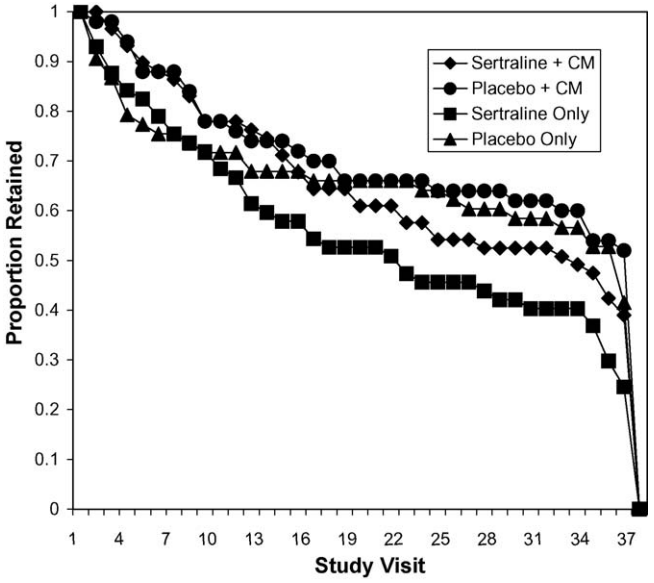

Fig. 3. Kaplan–Meier plot of study retention by treatment condition. Sertraline-only participants were retained in treatment for significantly less time than participants in all other treatment conditions (χ^2 (3) = 8.40, $p < 0.05$).

$p = 0.035$). When the four study conditions were collapsed to two (sertraline versus placebo), a strong trend was observed for significantly more participants receiving placebo (46.8%) to achieve at least three consecutive weeks of methamphetamine metabolite-free urine samples compared to participants receiving sertraline (34.2%; χ^2 (1) = 3.8, $p = 0.052$). Similarly, when the four study conditions were collapsed to participants receiving contingency management versus those not receiving contingency management, significantly more participants receiving contingency management (47.0%) achieved three consecutive weeks of methamphetamine abstinence than those not receiving contingency management (33.3%; χ^2 (1) = 4.4, $p = 0.036$).

3.3. Retention

A total of 116 participants (50.7%) completed all 14 weeks of the trial and the average length of stay during the 12 weeks of the medication phase across all conditions was 7.6 weeks. Survival analysis showed significantly fewer participants in the sertraline-only condition were retained over the medication phase of the study compared to participants in the other conditions (Fig. 3).

3.4. Methamphetamine craving

There were no statistically significant effects for sertraline, contingency management, or their interaction on craving ratings. There was, however, a significant effect of time on craving ratings with baseline VAS ratings decreasing significantly across conditions to the end of the trial ($M_{\text{baseline}} = 4.5$ (S.D. = 3.3)) to week 14 ($M_{\text{week 14}} = 2.7$ (S.D. = 3.2); $t(141) = 6.2$, $p < 0.001$).

3.5. Depressive symptoms

There were no statistically significant differences for sertraline, contingency management or their interaction in depression ratings over the clinical trial as tested using a GEE model. A significant effect of time across the four conditions was observed, however, with a decrease of nearly nine points on the BDI from baseline compared to ratings in week 14 ($M_{\text{baseline}} = 14.1$ (S.D. = 8.7), $M_{\text{week 14}} = 5.2$ (S.D. = 6.7); $t(153) = 12.18$, $p < 0.001$).

3.6. Clinic attendance and CM performance

Participants assigned to the sertraline-only condition attended significantly fewer of the relapse prevention groups ($M = 13.5$, S.D. = 11.4) compared to participants assigned to the other conditions (sertraline plus contingency management = 19.5, S.D. = 13.7; placebo plus contingency management = 20.9, S.D. = 14.0; and placebo-only = 18.3, S.D. = 13.2; $F(3,226) = 3.61$, $p = 0.014$). Participants in the sertraline plus contingency management condition averaged US$ 200 (S.D. = US$ 290), or 20.1% of the total possible earnings. The placebo plus contingency management condition averaged US$ 232 (S.D. = US$ 307), or 23.3% of the total possible earnings (non-significant difference).

3.7. Medication adherence and adverse events

A high percentage of study participants reported at least 80% adherence to study medication, with no statistically significant differences across the four groups (sertraline plus CM = 91.7%, sertraline-only = 85.2%, placebo plus CM = 91.7%, and placebo-only = 78.4%; χ^2 (3) = 5.5, $p = 0.139$). Participants receiving sertraline reported significantly more nausea and sexual, gastrointestinal, and anticholinergic side effects than participants receiving placebo (Table 2).

Table 2
Incidence of adverse events by sertraline or placebo conditions

Adverse event	Sertraline, $n = 120$, % (n)	Placebo, $n = 109$, % (n)
Nausea*	15.0 (18)	3.7 (4)
Diarrhea	13.3 (16)	10.1 (11)
Heartburn/indigestion	8.3 (10)	3.7 (4)
Anxiety	2.5 (3)	4.6 (5)
Increased MA craving	0.0 (0)	2.8 (3)
Depression	0.8 (1)	4.6 (5)
Fatigue	11.7 (14)	14.7 (16)
Urinary dysfunction	1.7 (2)	1.8 (2)
Body aches	5.0 (6)	7.3 (8)
Headache	22.5 (27)	14.7 (16)
Insomnia	13.3 (16)	12.8 (14)
Dry mouth	3.3 (4)	1.8 (2)
Sexual dysfunction**	6.7 (8)	0.9 (1)
Hypertension	1.7 (2)	0.9 (1)
All gastrointestinal***	26.7 (32)	14.7 (16)
All anticholinergic****	38.3 (46)	24.8 (27)

* χ^2 (1) = 8.4, $p = 0.004$.
** χ^2 (1) = 5.0, $p = 0.025$.
*** χ^2 (1) = 5.0, $p = 0.026$.
**** χ^2 (1) = 4.8, $p = 0.028$.

4. Discussion

Study results did not confirm project hypotheses. There were no statistically significant main or interaction effects for the medication or behavioral therapies delivered in this trial along measures of methamphetamine use, retention, drug craving, depression, or medication adherence. Moreover, sertraline appeared to worsen methamphetamine use, as indicated by the greater number of urine samples positive for methamphetamine metabolites and reduced likelihood of achieving three consecutive weeks of methamphetamine abstinence for participants assigned to the sertraline-only condition compared to the other three conditions. Participants in the sertraline-only condition were also significantly more likely to terminate from the study prematurely compared to participants in other study conditions.

Taken together, these data demonstrate multiple indices by which sertraline not only does not improve methamphetamine use outcomes over placebo, but likely dampens effects of behavioral therapies for treatment of methamphetamine dependence. The finding that the sertraline-only condition significantly under-performed the placebo-only condition suggests that effects of the relapse prevention model used as a psychosocial counseling platform in this study may have been dampened by sertraline.

There are significant clinical implications of these findings. At a minimum, clinicians should be advised to avoid the use of sertraline as a first line pharmacotherapy for methamphetamine-dependent individuals presenting for care and who may complain of depression, unless an underlying depressive disorder is definitively diagnosed. Moreover, these results, together with the failures of fluoxetine (Batki et al., 1999) and paroxetine (Piasecki et al., 2003) to demonstrate utility for treating methamphetamine dependence, suggest that the entire class of SSRI's may be ineffective, and that further evaluation of these medications for this indication is thus unwarranted. In lieu of providing a pharmacotherapy, a more appropriate course would emphasize behavioral interventions that can assist individuals in initiating and sustaining abstinence from methamphetamine (Shoptaw et al., 2005; Rawson et al., 2004). This strategy might well relieve reported depressive symptoms likely to be methamphetamine-induced as well (Peck et al., 2005b).

A surprising outcome is the relatively anemic response to the contingency management protocol fielded in this study. Albeit longer by 4 weeks and involving a sample of gay and bisexual male methamphetamine abusers, another study reported (Shoptaw et al., 2005) that contingency management combined with identical Matrix Model relapse prevention groups yielded an average payout of US$ 662, or nearly three times that observed in this trial.

Also intriguing is that no clinically or statistically significant effects were observed for sertraline in reducing ratings of depressive symptoms over the active medication period. This finding provides support for Newton's suggestion (Newton et al., 2004) that the depressive symptoms commonly reported in early abstinence from methamphetamine are likely to represent a syndrome distinct from that of primary, non-substance induced depressive disorders. Furthermore, relapse prevention and contingency management-based interventions have been shown to greatly reduce reported depressive symptoms among gay and bisexual methamphetamine abusers (Peck et al., 2005b). Based on the current evidence, behavioral interventions designed to reduce methamphetamine abuse remain the optimal method for eliminating depressive complaints secondary to withdrawal from methamphetamine.

The sertraline dosage of 100 mg/day evaluated in this study represents one-half the maximum recommended dose for major depressive disorder and anxiety disorders. It is possible that a higher dose might have demonstrated efficacy for reducing methamphetamine use. However, given that participants in the sertraline conditions reported significantly more adverse events than those in the placebo conditions, it is likely that a higher dose would have produced an even greater incidence of side effects and related premature study terminations.

This study represents the largest controlled clinical trial of combined medication and behavioral therapies for methamphetamine-dependent individuals. Findings provide no rationale for continuing to evaluate sertraline, or SSRI's as a class, as pharmacotherapy for methamphetamine dependence. Despite the reported high rates of medication adherence across study conditions, it is always possible that the failure of sertraline to reduce methamphetamine use was due to poor adherence. If this were the case, however, the suitability of sertraline as a treatment for methamphetamine dependence is further called into question; the utility of a pharmacotherapy is negligible if it produces adverse effects severe enough that individuals will not take the medication consistently. Findings from the project provide evidence to support contingency management as a behavioral therapy for methamphetamine dependence.

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