

Methylphenidate Treatment for Cocaine Abusers With Adult Attention-Deficit/Hyperactivity Disorder: A Pilot Study

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Background: Attention-deficit/hyperactivity disorder (ADHD) is common among cocaine abusers seeking treatment. This open trial was carried out to assess the efficacy of sustained-release methylphenidate for the treatment of cocaine abuse among individuals with ADHD.

Method: Twelve patients who met DSM-IV diagnostic criteria for adult ADHD and cocaine dependence were entered into a 12-week trial of divided daily doses of sustained-release methylphenidate ranging from 40 to 80 mg. In addition to the pharmacotherapy, patients also received individual weekly relapse prevention therapy. Individuals were assessed weekly for ADHD symptoms; vital signs and urine toxicologies were obtained 3 times a week.

Results: Of the 12 patients entered, 10 completed at least 8 weeks of the study and 8 completed the entire study. Using both a semistructured clinical interview and a self-report assessment, patients reported reductions in attention difficulties, hyperactivity, and impulsivity. Self-reported cocaine use and craving decreased significantly. More importantly, cocaine use, confirmed by urine toxicologies, also decreased significantly.

Conclusion: These preliminary data suggest that under close supervision, the combined intervention of sustained-release methylphenidate and relapse prevention therapy may be effective in treating individuals with both adult ADHD and cocaine dependence.

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Despite the fact that over 30 medications have been tested for the treatment of cocaine dependence, treatment remains inadequate, perhaps owing in part to untreated comorbid disorders. At particular risk for early dropout and/or poor treatment outcome may be those individuals with adult attention-deficit/hyperactivity disorder (ADHD). Recent studies confirm that individuals with ADHD symptoms persisting into adulthood are at greatest risk for having a substance use disorder.^{1,2} Consistent with this, 35% of cocaine abusers seeking treatment had a history of childhood ADHD,³ and approximately 15% of cocaine abusers seeking treatment may have adult ADHD (F.R.L., S.M.E., H.D.K., unpublished observations).

Psychostimulants, particularly methylphenidate, are the most efficacious and commonly prescribed medications used to treat childhood ADHD.⁴ Seven studies have evaluated the efficacy of methylphenidate in adults with ADHD, with the majority reporting an improvement in ADHD symptoms.^{5–11} The studies that have shown the best response to methylphenidate have used large doses.^{9–11} Spencer and colleagues¹¹ found that 78% of patients receiving methylphenidate (up to 1 mg/kg per day) had a meaningful improvement in ADHD symptoms compared with only 4% of those receiving placebo.

Data are limited regarding the impact of pharmacologic treatment for substance abusers with adult ADHD. Although most placebo-controlled trials have been designed to assess pharmacotherapies in adult ADHD without substance abuse, 2 double-blind, placebo-controlled trials included a small number of substance abusers (≤ 8 patients) who received methylphenidate.^{8,11} Both studies found that substance abusers who received methylphenidate were more likely to have a reduction in ADHD symptoms than those who received placebo. However, neither study reported on whether methylphenidate produced changes in drug use.

At present, there have been 5 case reports suggesting that methylphenidate, pemoline, or bromocriptine might be useful for cocaine abusers with adult ADHD.^{12–16} One study used a double-blind crossover design to assess the efficacy of bromocriptine in 2 patients.¹⁷ Although the authors concluded that bromocriptine was not effective for adult ADHD, the small sample precludes any adequate evaluation of the medication's efficacy. Schubiner and

colleagues¹⁸ have found that methylphenidate may also be effective for alcoholics with ADHD. None of these studies routinely collected urine toxicologies or assessed ADHD symptoms using clinical research instruments. Given that previous case reports and double-blind studies suggest that methylphenidate is useful in treating ADHD symptoms for substance abusers with adult ADHD, the next logical step is to determine if methylphenidate reduces cocaine use. Therefore, the purpose of this study was to further evaluate the safety, feasibility, and potential efficacy of methylphenidate for the treatment of both adult ADHD and cocaine abuse.

METHOD

Patients

One hundred nine callers responded to an advertisement offering free treatment for ADHD and cocaine abuse within a research setting. Thirty-two met initial screening criteria and came to the clinic for an initial assessment. Two self-report ratings were used to assess individuals for a possible diagnosis of childhood and adult ADHD: (1) the Wender Utah Rating Scale (WURS)¹⁹ and (2) the Adult Behavior Checklist (ABC).²⁰ The WURS is a retrospective rating scale developed for adults consisting of 25 items, rated on a scale of 0 (not at all) to 4 (very much); patients rate the items describing their childhood behavior. A total score ≥ 36 suggests that childhood ADHD may be present. The ABC is an 18-item self-report questionnaire that uses all of the DSM-IV symptoms for ADHD, and each item is rated on a scale of 0 (not at all) to 3 (very much) for a maximum score of 54. Nine items pertain to inattention and 9 items pertain to hyperactive-impulsive behavior. Scores suggestive of ADHD are obtained in 1 of 3 ways: (1) 6 of the total 18 items are rated as 2 or 3, (2) 3 of the inattentive items are rated as 2 or 3, or (3) 4 of the hyperactive-impulsive items are rated as 2 or 3.

Of the 32 potential patients given the 2 screening instruments, 24 had elevated cutoff scores on the WURS and/or the ABC. Because these screening instruments do not guarantee that an individual has childhood or adult ADHD, these patients were then assessed by experienced interviewers, a master's-level psychologist or psychiatrist (F.R.L.), using the Structured Clinical Interview for DSM-IV Axis I and II Disorders (SCID-I and SCID-II).^{21,22} In addition to the standard SCID, a KID-SCID module for ADHD, along with a modified adult ADHD module, was used as the primary method for diagnosing childhood and adult ADHD. Both of these modules adhere strictly to DSM-IV criteria and use the same SCID-like format as the other commonly used SCID modules. Of the 24 patients interviewed, 17 (71%) met DSM-IV criteria for adult ADHD based on the clinical interview. The Utah Criteria,²³ an alternative approach used to diag-

nose adult ADHD, were not used to include or exclude individuals from study participation. Instead, we wanted to determine whether individuals enrolled in the study who met DSM-IV criteria for adult ADHD also met the diagnosis of ADHD based on the Utah Criteria. The Utah Criteria incorporate additional symptoms to those described in DSM-IV and require the presence of both inattentive *and* hyperactive symptoms; the DSM-IV criteria require the presence of inattentive symptoms *or* hyperactive symptoms. Medical stability was determined by a physical examination, detailed medical history, electrocardiogram, and laboratory tests (complete blood cell count with differential, electrolytes, blood urea nitrogen [BUN], creatinine, liver function tests, and thyroid function tests). Pregnancy in women was determined by a blood pregnancy test. Women who were pregnant or nursing were excluded from the study.

All patients signed 2 consent forms approved by the Institutional Review Board of the New York State Psychiatric Institute (NYSPI) prior to study entry. The first consent form allowed us to screen patients for the study protocol. The second consent form was given to patients who met inclusion criteria and were offered admission into the research study. Patients were told that the purpose of the study was to evaluate the efficacy of 2 treatment medications for adult ADHD and cocaine abuse. Patients were also told that they would be receiving only 1 study medication, either methylphenidate or desipramine, during the entire 12-week trial. It was emphasized to all potential patients that both medications had shown promise in treating adult ADHD but that it remained unclear if these medications had clinical utility for cocaine addiction.

Treatment

During the 12-week outpatient study, patients came to the cocaine clinic at the NYSPI 3 times each week to receive medication, provide a urine sample for drug screening, have vital signs taken, and complete self-report drug use and craving questionnaires. Over a period of 2 to 4 weeks, patients were stabilized on 40 to 80 mg/day of sustained-release methylphenidate (divided doses twice a day) based on clinical efficacy and side effects. (Methylphenidate was gradually increased to 40 mg/day and switched to the sustained-release formulation to reduce abuse potential in this population and eliminate the need for multiple daily dosing.) All medication was prepared in blue-colored gelatin capsules with lactose powder as the filler; placebo capsules contained only lactose powder. Four capsules were provided to the patients for each study day in containers marked by both day of the week (e.g., Monday, Tuesday) and time of day (e.g., a.m., p.m.); patients were instructed to take 2 capsules in the morning and 2 in the afternoon. All patients received enough medication to last until their next scheduled appointment.

All patients received standardized behavioral treatment throughout the study. To ensure that all patients received the same "dose" of relapse prevention therapy, a structured relapse prevention manual designed by Carroll and colleagues²⁴ was used. For all of the patients enrolled in the study, the same master's-level psychologist provided the weekly individual treatment. The sessions focused on identifying individual high-risk situations for cocaine use and developing cognitive and behavioral strategies to avoid cocaine use in those situations. The impact of ADHD symptoms on cocaine use was also incorporated into sessions whenever pertinent. Sessions were videotaped (with informed consent from the patients) and reviewed in staff supervision.

Assessments

Baseline assessments (i.e., those made during screening) were carried out before initiation of treatment and then repeated throughout the study. Vital signs were monitored and a side effects checklist was given to patients at each visit (3 times a week). Blood was drawn once a week for assessment of methylphenidate levels. There were 2 major types of outcome measures: those related to drug abuse and those related to ADHD symptoms. Weekly assessments of ADHD symptoms were carried out using the Targeted Attention Deficit Disorder Symptoms scale (TADDS)²³ and the ABC.²⁰ The TADDS is a semistructured interview that consists of the 7 target symptoms that are the defining attributes of the Utah Criteria,²³ an alternative method to diagnosing adult ADHD. Anchor points range from 0 (none) to 4 (very much) on 7 different domains that have been described as areas of particular difficulty for those with adult ADHD: attention difficulties, hyperactivity, temper, mood instability, overreactivity, disorganization, and impulsivity. The ABC,¹⁸ a self-report questionnaire, was previously described above. All of these instruments were also completed at the 3-month follow-up assessment.

Assessments relevant to drug use included the Addiction Severity Index (ASI),²⁵ a cocaine-craving questionnaire, several cocaine-craving visual analogue scales, and urine toxicology results. The ASI is a 140-item structured clinical interview that uses both subjective and objective information to make severity ratings on a 10-point scale in 6 domains, including substance abuse. The ASI was conducted at baseline, week 6, week 12, and at the 3-month follow-up assessment. Self-reported drug use was assessed using data collected by the ASI, which provides information regarding frequency of use for various classes of substances and route of consumption in the past 30 days. In addition, at each visit, a staff member reviewed all drug use with the patient since the last visit. When discrepancies occurred, the higher frequency of use was utilized. Cocaine craving and severity of drug use were assessed using several visual analogue scales. Pa-

tients rated their craving during the past 24 hours and since their last clinic visit. Patients also submitted urine samples 3 times per week, and these were analyzed for cocaine using a semiquantitative analysis. Due to the uncertainties surrounding the interpretation of quantitative levels, standard National Institute on Drug Abuse (NIDA) guidelines for cutoff points (e.g., 300 ng/mL for cocaine) were used.

Data Analysis

For the 10 patients who completed at least 8 weeks of the study, paired *t* tests were used to examine differences for each outcome measure assessing ADHD symptoms and drug use. Mean scores for each of the TADDS subscales and the ABC were computed using the screening assessment and the first assessment in the study compared with the last 2 assessments in the study. ASI subscale severity scores and the frequency of self-reported days of cocaine use in the month prior to study entry were compared with the same measures from the last month enrolled in the study. Percentages of cocaine-positive urine samples and visual analogue ratings of craving were calculated for each patient for the screening week and the first week in the study compared with the same measures from the last 2 weeks in the study.

RESULTS

Of the 17 patients who met criteria for adult ADHD based on the SCID, 13 met all additional study criteria and gave signed informed consent for the treatment study. Twelve were initiated with study medication. Of these, 2 patients dropped out within the first 4 study weeks; 1 patient was arrested and chose not to return to treatment. The other underreported the extent of his heroin use; he was offered a referral for opiate detoxification but refused this option and was dropped from the study.

For the 10 patients who completed at least 8 weeks of the study, 6 were men (5 white, 1 black) and 4 were women (3 white, 1 black). The mean \pm SE age was 34 ± 1.4 years, and the mean \pm SE age at onset of regular cocaine use was 22 ± 1.0 years (range, 16–26 years). Before treatment, the mean \pm SE cost of weekly cocaine use was $\$380 \pm \155 (range, $\$25$ – $\$1500$ /week) and the primary route of administration was intranasal (80%). No one reported prior treatment with methylphenidate as a child or as an adult. Psychiatric comorbidity was common among this population; 40% had a current Axis I anxiety disorder that was not substance related, and 60% had at least one DSM-IV Axis II disorder, most commonly antisocial personality disorder or borderline personality disorder. Although study eligibility was not based on meeting the Utah Criteria for adult ADHD, 6 of the 10 patients also had adult ADHD based on the Utah Criteria. Three of

Table 1. Paired t Test Comparison for Scores on the 7 Subscales of the TADDS in 10 Cocaine Abusers Treated With Methylphenidate*

Subscales	First 2 Assessments ^a		Last 2 Assessments		p
	Mean	SE	Mean	SE	
Attention	2.70	0.24	1.15	0.20	< .0001
Hyperactivity	2.10	0.28	1.25	0.22	.019
Temper	1.95	0.28	1.10	0.21	.018
Mood lability	1.65	0.26	1.20	0.19	NS
Over reactivity	1.95	0.25	1.20	0.24	.034
Disorganization	2.75	0.26	1.70	0.22	.003
Impulsivity	2.25	0.23	1.35	0.23	.007

*For the TADDS, 0 = no difficulty, 4 = very much difficulty. Abbreviations: NS = not significant, TADDS = Targeted Attention Deficit Disorder Symptom scale.
^aScreening assessment and first assessment in the study.

the remaining 4 patients did not meet Utah Criteria because they had inattentive symptoms but not hyperactive symptoms.

For the 10 patients who were maintained on sustained-release methylphenidate, the maintenance doses ranged from 40 to 80 mg/day in 2 divided doses: 1 patient was maintained on 40 mg, 4 were maintained on 60 mg, and 5 were maintained on 80 mg. The most frequently reported side effects were dry mouth, increased heart rate, jitteriness, and agitation. No patient was discontinued because of side effects. There were no clinically significant changes in the results of routine laboratory tests of blood, which was drawn monthly.

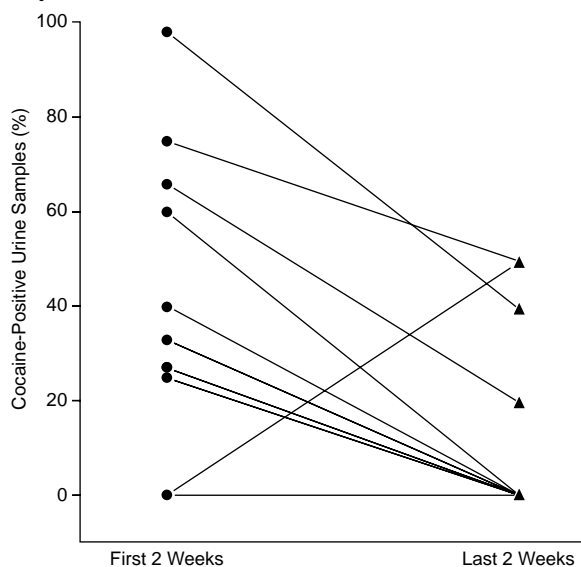
Treatment Outcome: ADHD Measures

As shown in Table 1, significant improvements in ADHD symptoms were observed using the TADDS. All of the TADDS subscales showed significant improvement with the exception of mood lability. Similarly, the self-reported ABC scores, completed for 8 patients, showed a significant reduction in ADHD symptoms ($t = 2.4, df = 7, p < .05$; data not shown). Specifically, ABC scores obtained during the screening and the first week of the study, when compared with scores from the last 2 weeks of the study, dropped by almost 50% (35.6 ± 3.4 to 18.2 ± 4.2 , respectively).

Treatment Outcome: Drug Use Severity, Cocaine Craving, and Cocaine Use

Most patients reported that cocaine craving became minimal within the first 3 weeks of study entry. On the basis of the ASI and the recent drug use questionnaire, self-reported frequency of cocaine use during the 4 weeks before study entry decreased significantly compared with use during the last 4 weeks of study enrollment (9.8 ± 2.7 days to 1.1 ± 0.5 days; $t = 3.59, df = 9, p < .006$). Similarly, ASI drug use severity ratings also decreased significantly (6.0 ± 0.7 to 2.5 ± 1.1 ; $t = 3.0, df = 9, p < .02$). On the basis of a visual analogue scale, cocaine craving was signifi-

Figure 1. Percentage of Cocaine-Positive Urine Samples for Individual Patients During the Screening Week and the First Week of the Study Compared With the Last 2 Weeks of the Study*



*Total percentage of cocaine-positive urine samples decreased significantly from the screening week and first week of the study to the last 2 weeks of the study ($t = 2.1, df = 9, p < .05$).

cantly greater during the screening and the first week of the study compared with that during the last 2 weeks of the study ($t = 3.2, df = 9, p = .01$). More importantly, Figure 1 shows that the percentage of cocaine-positive urine samples dropped significantly ($t = 2.1, df = 9, p < .05$) when the screening week and the first week of the study were compared with the last 2 weeks in the study for individual patients. Of note, 85% of all urine samples were collected; the lowest rate was 69% for 1 patient.

Overall, patients kept 91% of the clinic appointments; thus, few medication doses were missed due to lack of attendance. Weekly blood methylphenidate levels were obtained to determine if self-reported medication compliance correlated with actual ingestion of medication. For the 81 methylphenidate levels determined over the course of the study, there were only 4 instances in which the patient reported taking medication and no detectable methylphenidate level was obtained. Because blood was drawn at varying times since the last medication dose, blood methylphenidate levels were used only to assess compliance.

Of the 10 patients who completed at least 8 weeks of the study, 7 were reachable for the 3-month follow-up visit. Three of these patients were still being treated with methylphenidate at the time of the follow-up visit, and each of their urine samples was negative for cocaine. The remaining 4 patients were not being treated with medication, and 2 of these patients submitted cocaine-positive urine samples at the follow-up visit.

DISCUSSION

The results of this study suggest that sustained-release methylphenidate, in daily doses up to 80 mg, may reduce ADHD symptoms, cocaine craving, and cocaine use among cocaine abusers with ADHD. Several possible relationships may exist between ADHD and cocaine abuse, so it is unlikely that only one approach, i.e., pharmacotherapy, will provide adequate treatment for cocaine abusers with adult ADHD.²⁶ Effective medication may help reduce impulsivity or improve concentration, such that relapse prevention or other therapeutic techniques can be more effectively utilized.

Because methylphenidate has abuse liability, its use is somewhat controversial, particularly among substance abusers. Theoretically, methylphenidate might be diverted (i.e., other individuals might take the medication and/or the patient might sell the medication to others), increase cocaine craving and/or use,²⁷ or produce significant cardiovascular effects when combined with cocaine. None of these issues posed a significant problem during the course of the study. Blood methylphenidate levels were assessed weekly, and individuals, with rare exception, accurately reported whether or not they ingested their medications. Clearly, in a placebo-controlled trial, it would be crucial to monitor blood levels to help ensure that patients were compliant and to discontinue medication if diversion of methylphenidate is suspected.

The effectiveness of methylphenidate in reducing cocaine abuse in this study may have been influenced, or solely produced, by several variables, including (1) the open, rather than double-blind, design; (2) substantial support provided by frequent staff interactions; and (3) the therapeutic benefit provided by individual relapse prevention therapy. Repeatedly, medications that have shown promise as potential treatments for cocaine addiction in open trials²⁸⁻³⁰ have been shown to be ineffective in larger, double-blind trials.³¹⁻³⁴ Therefore, the findings of this study need to be viewed cautiously. Of note, we are currently conducting another pharmacologic treatment study of cocaine abusers without ADHD, who have similar staff interactions and the same weekly therapy, yet, the results do not appear promising (F.R.L., S.M.E., H.D.K., unpublished observations). Although it might seem that a pharmacologic trial without other therapeutic interventions and with limited staff contact might be a "cleaner" way to assess the utility of a pharmacotherapy, it is becoming increasingly clear that behavioral therapy combined with pharmacologic treatment enhances both treatment retention and medication compliance.^{35,36} If we wish to adequately assess the efficacy of new pharmacologic approaches for cocaine dependence, methods that enhance treatment compliance are crucial.

At present, few promising treatments exist for cocaine addiction. In this study, we were able to engage a

difficult-to-treat population and demonstrate clinically significant reductions in ADHD symptoms and cocaine use. These findings suggest that further study of methylphenidate for this dually diagnosed population under double-blind conditions is warranted.

Drug names: bromocriptine (Parlodel), desipramine (Norpramin and others), methylphenidate (Ritalin), pemoline (Cylert).

REFERENCES

- Mannuzza S, Klein RG, Bonagura N, et al. Adult outcome of hyperactive boys: educational achievement, occupational rank, and psychiatric status. *Arch Gen Psychiatry* 1993;48:77-83
- Biederman J, Wilens T, Mick E, et al. Psychoactive substance use disorders in adults with attention deficit hyperactivity disorder (ADHD): effects of ADHD and psychiatric comorbidity. *Am J Psychiatry* 1995;152:1652-1658
- Rounsaville BJ, Anton SF, Carroll K, et al. Psychiatric diagnoses of treatment-seeking cocaine abusers. *Arch Gen Psychiatry* 1991;48:43-51
- Greenhill LL. Pharmacotherapy: stimulants. In: Weiss G, ed. *Child and Adolescent Psychiatric Clinics of North America*. Philadelphia, Pa: WB Saunders Co; 1992:411-447
- Wood DR, Reimherr FW, Wender PH, et al. Diagnosis and treatment of minimal brain dysfunction in adults. *Arch Gen Psychiatry* 1976;33:1453-1460
- Wender PH, Reimherr FW, Wood DR. Attention deficit disorder ("minimal brain dysfunction") in adults: a replication study of diagnosis and drug treatment. *Arch Gen Psychiatry* 1981;38:449-456
- Wender PH, Reimherr FW, Wood D, et al. A controlled study of methylphenidate in the treatment of attention deficit disorder, residual type, in adults. *Am J Psychiatry* 1985;142:547-552
- Mattes JA, Boswell L, Oliver H. Methylphenidate effects on symptoms of attention deficit disorder in adults. *Arch Gen Psychiatry* 1984;41:1059-1063
- Gualtieri CT, Ondrusek MG, Finley C. Attention deficit disorder in adults. *Clin Neuropharmacol* 1985;8:343-356
- Shekim WO, Asarnow RF, Hess E, et al. A clinical and demographic profile of a sample of adults with attention deficit hyperactivity disorder, residual state. *Compr Psychiatry* 1990;31:416-425
- Spencer T, Wilens T, Biederman J, et al. A double-blind, crossover comparison of methylphenidate and placebo in adults with childhood-onset attention-deficit hyperactivity disorder. *Arch Gen Psychiatry* 1995;52:434-443
- Khantzian EJ. An extreme case of cocaine dependence and marked improvement with methylphenidate treatment. *Am J Psychiatry* 1983;140:484-485
- Khantzian EJ, Gawin FH, Kleber HD, et al. Methylphenidate (Ritalin) treatment for cocaine dependence: a preliminary report. *J Subst Abuse Treat* 1984;1:107-112
- Weiss RD, Pope HG, Mirin SM. Treatment of chronic cocaine abuse and attention deficit disorder, residual type, with magnesium pemoline. *Drug Alcohol Depend* 1985;15:69-72
- Cocores JA, Davies RK, Mueller PS, et al. Cocaine abuse and adult attention deficit disorder. *J Clin Psychiatry* 1987;48:376-377
- Cocores JA, Patel MD, Gold MS, et al. Cocaine abuse, attention deficit disorder, and bipolar disorder. *J Nerv Ment Dis* 1987;175:431-432
- Cavanagh R, Clifford JST, Gregory WL. The use of bromocriptine for the treatment of attention deficit disorder in two chemically dependent patients. *J Psychoactive Drugs* 1989;21:217-220
- Schubiner H, Tzelepis A, Isaacson JH, et al. The dual diagnosis of attention-deficit/hyperactivity disorder and substance abuse: case reports and literature review. *J Clin Psychiatry* 1995;56:146-150
- Ward MF, Wender PH, Reimherr FW. The Wender Utah Rating Scale (WURS): an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry* 1993;150:885-890
- Murphy K, Barkley R. Prevalence of DSM-IV symptoms of ADHD in adult licensed drivers. *J Attention Disord* 1996;1:147-161
- First MB, Spitzer RL, Gibbon M, et al. *Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-IP, Version 2.0)*. New York, NY: Biometric Research, New York State Psychiatric Institute; 1995

22. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II, Version 2.0). New York, NY: Biometric Research, New York State Psychiatric Institute; 1994
23. Wender PH. Attention-Deficit Hyperactivity Disorder in Adults. Oxford, England: Oxford University Press; 1995
24. Carroll KM, Rounsaville BJ, Gordon LT, et al. Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. *Arch Gen Psychiatry* 1994;51:177-187
25. McLellan AT, Luborsky L, Woody DR, et al. An improved instrument for substance abuse patients: the Addiction Severity Index. *J Nerv Ment Dis* 1980;168:26-33
26. Levin FR, Kleber HD. Attention-deficit hyperactivity disorder and substance abuse: relationships and implications for treatment. *Harv Rev Psychiatry* 1995;2:246-258
27. Gawin F, Riordan C, Kleber HD. Methylphenidate treatment of cocaine abusers without attention deficit disorder: a negative report. *Am J Drug Alcohol Abuse* 1985;11:193-197
28. Handelsman L, Chordia PL, Escovar IL, et al. Amantadine for the treatment of cocaine dependence in methadone-maintained patients [letter]. *Am J Psychiatry* 1988;145:533
29. Margolin A, Kosten TR, Petriakis IL, et al. Bupropion reduces cocaine abuse in methadone-maintained patients [letter]. *Arch Gen Psychiatry* 1991;48:87
30. Halikas J, Kemp K, Kuhn K, et al. Carbamazepine for cocaine addiction? *Lancet* 1989;1:623-624
31. Kampman K, Volpicelli JR, Alterman A, et al. Amantadine in the early treatment of cocaine dependence: a double-blind, placebo-controlled trial. *Drug Alcohol Depend* 1996;41:25-33
32. Montoya ID, Levin FR, Fudala PJ, et al. A double-blind comparison of carbamazepine and placebo for treatment of cocaine dependence. *Drug Alcohol Depend* 1995;38:213-219
33. Margolin A, Kosten TR, Avants SK, et al. A multicenter trial of bupropion for cocaine dependence in methadone-maintained patients. *Drug Alcohol Depend* 1995;40:125-131
34. Kosten TR. Pharmacotherapies. In: Kosten TR, Kleber HD, eds. *Clinician's Guide to Cocaine Addiction: Theory, Research, and Treatment*. New York, NY: The Guilford Press; 1992:273-289
35. Callahan EJ, Rawson RA, McCleave B, et al. The treatment of heroin addiction: naltrexone alone and with behavior therapy. *Int J Addict* 1980;15:795-807
36. O'Malley SS, Carroll KM. Psychotherapeutic considerations in pharmacologic trials. *Alcohol Clin Exp Res* 1996;20:17A-22A

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