

A Randomized Controlled Trial of Auricular Acupuncture for Cocaine Dependence

S. Kelly Avants, PhD; Arthur Margolin, PhD; Theodore R. Holford, PhD; Thomas R. Kosten, MD

Background: Partly because of a lack of a conventional, effective treatment for cocaine addiction, auricular acupuncture is used to treat this disorder in numerous drug treatment facilities across the country for both primary cocaine-dependent and opiate-dependent populations.

Objective: To evaluate the effectiveness of auricular acupuncture for the treatment of cocaine addiction.

Methods: Eighty-two cocaine-dependent, methadone-maintained patients were randomly assigned to 1 of 3 conditions: auricular acupuncture, a needle-insertion control condition, or a no-needle relaxation control. Treatment sessions were provided 5 times weekly for 8 weeks. The primary outcome was cocaine use assessed

by 3-times-weekly urine toxicology screens.

Results: Longitudinal analysis of the urine data for the intent-to-treat sample showed that patients assigned to acupuncture were significantly more likely to provide cocaine-negative urine samples relative to both the relaxation control (odds ratio, 3.41; 95% confidence interval, 1.33-8.72; $P = .01$) and the needle-insertion control (odds ratio, 2.40; 95% confidence interval, 1.00-5.75; $P = .05$).

Conclusions: Findings from the current study suggest that acupuncture shows promise for the treatment of cocaine dependence. Further investigation of this treatment modality appears to be warranted.

Arch Intern Med. 2000;160:2305-2312

USE OF cocaine continues to be a serious problem in the United States. The 1998 National Household Survey on Drug Abuse reported 1.8 million current users, with a significant increase in use among those aged 18 to 25 years relative to the previous year.¹ At present, there are few conventional treatments with demonstrated efficacy available for the treatment of this disorder. Given the lack of conventional treatments, an alternative therapy—auricular acupuncture, as codified by the National Acupuncture Detoxification Association (NADA)²—is in widespread use in drug treatment facilities across the country.³ Although a number of preliminary studies investigating the effectiveness of acupuncture for the treatment of cocaine addiction have reported positive results,⁴ findings from controlled studies have to date been inconclusive, with some studies reporting positive treatment effects for acupuncture,⁵⁻⁷ while others have reported finding no difference between acupuncture and controls.⁸⁻¹²

One impediment to determining the effectiveness of auricular acupuncture stems from the complexity of investigating this treatment modality in controlled

studies.^{13,14} Acupuncture is a procedure, and developing controls for procedures and testing them under blinded conditions offers numerous problems.^{15,16} In planning the current study, we deemed it important to control for both nonspecific factors, such as monitoring of drug use, completion of questionnaires, and staff attention, and specific factors that necessarily attend an acupuncture treatment and that may confound interpretation of findings.¹⁷ For example, acupuncture treatments typically involve patients reposing in a quiet setting under relaxing conditions. Because relaxation has been associated with reduced drug craving,^{18,19} which may in turn reduce drug use and have other beneficial effects independent of any presumed acupuncture effects, a nonneedle relaxation protocol was developed to control for these nonspecific effects of acupuncture treatments.

In addition to possible relaxation effects induced by the treatment context, insertion of needles into the body is a potentially impressive ritual that may elicit a beneficial placebo response in drug users, independent of an acupuncture-specific mechanism.²⁰ To control for this aspect of the acupuncture treatment, acupuncture studies have used needle insertion into “sham” points, usually stipu-

From the Division of Substance Abuse, Department of Psychiatry (Drs Avants, Margolin, and Kosten), and Division of Biostatistics, School of Epidemiology and Public Health (Dr Holford), Yale University School of Medicine, and Department of Psychiatry, Veterans Affairs Connecticut Healthcare Center (Dr Kosten), New Haven.

PATIENTS AND METHODS

PARTICIPANTS

Participants were 82 cocaine- and opioid-dependent patients enrolled in an inner-city MMP who were referred to the study because of their unremitting cocaine use. This sample size was projected to provide sufficient power (0.80) to detect a moderate to large treatment effect (0.35) among the treatment conditions. The research protocol was approved by the Human Investigation Committee of Yale University School of Medicine, New Haven, Conn, and all participants provided signed informed consent to participate in the study.

ENTRANCE AND DISCONTINUATION CRITERIA

Inclusion criteria were (1) age of at least 18 years; (2) enrollment in an MMP and maintenance on a stable dose of methadone; (3) meeting criteria for cocaine dependence according to the Structured Clinical Interview for DSM-IV²⁵; and (4) evidence of recent cocaine use, as follows: (a) provision of a cocaine-positive urine screen at time of screening; (b) self-reported cocaine use the week before screening; or (c) provision of cocaine-positive urine screen within 2 weeks before screening. Exclusion criteria were as follows: (1) dependence on any substance other than opiates, cocaine, or nicotine; (2) current treatment for cocaine dependence; (3) current use of a psychotropic medication, unless maintained on a regimen of this medication for at least 90 days; (4) current acupuncture treatment or use of acupuncture in the previous 30 days; and (5) active suicidal or psychotic status. The intent-to-treat sample included all patients who were randomly assigned to treatment. Patients who failed to attend 3 of the first 8 sessions, as well as those who attended less than 1 session per week thereafter, were discontinued from the study and coded as *noncompleters*.

RANDOMIZATION

After completion of each patient's screening and intake interviews, a staff member generated the treatment assignment for that patient by means of a computer-based, randomization procedure,²⁶ programmed to balance the conditions on sex, race, and human immunodeficiency virus serostatus. In an orientation session, patients were informed of their treatment assignment, and the treatment was described by means of a standardized script. To enhance the credibility of the control conditions, patients were encouraged to view all of the study treatments as ways to reduce stress, with attendant benefits. Patients assigned to relaxation were additionally provided with instruction concerning the relaxation protocol to be provided. Treatment commenced on the Monday after randomization. The flow diagram in **Figure 1** illustrates the patients' progress through the trial.

TREATMENT CONDITIONS

NADA Auricular Acupuncture Protocol

As originally formulated, the NADA protocol specified needle insertion into 5 auricular zones; however, as practiced

clinically, the number of needles inserted bilaterally ranges from 3 to 5. In the current study, needles were inserted into the auricles bilaterally at 4 NADA-specified zones: *sympathetic*, located in the deltoid fossa at the junction of the infra-antihelix crus and the medial order of the helix; *lung*, located in the center of the cavum concha; *liver*, located in the posterior to upper portion of the helix crus; and *shen men*, located in the inferior corner of the bifurcating point of the antihelix. Needles were inserted into the cartilage at each point such that they were perpendicular to the surface of the ear, and entered the cartilage to a depth of between 1 and 3 mm. Needles were 0.20 mm wide and 15 mm long, stainless steel, and disposable; sterilized with ethylene oxide gas; and individually packaged in sterile containers (Seirin Co Ltd, Shimizu-City, Japan).

Auricular Needle-Insertion Control Condition

Four needles of the same type and size used for the active acupuncture treatment were inserted into the helix of the auricles bilaterally at 3 zones not commonly used for the treatment of any disorder. Two needles were inserted into zone 1, located on the helix from the high point of the helix to just above the superior border of Darwin's tubercle, on the anteroposterior dividing line border of the auricle; 1 needle was inserted into zone 2, located on the helix at the level of Darwin's tubercle, from just below the superior order of the tubercle to just above the inferior order of the tubercle, on the anteroposterior dividing line border of the auricle; and 1 needle was inserted into zone 3, located from just below the inferior order of Darwin's tubercle to approximately level with the end of the crus of the helix, on the anteroposterior dividing line border of the auricle. To further minimize the possibility of providing an active treatment, care was taken not to insert needles in the "liver Yang" points, which are located near these regions. Furthermore, needles were not inserted into the cartilage at each point; rather, they were inserted subcutaneously, at an oblique angle.

Relaxation Control Condition

This condition consisted of viewing commercially available videos, on a large-screen (30-inch [76.2 cm]) television, depicting relaxation strategies that had been described during orientation, as well as relaxing visual imagery (eg, nature scenes) and music. For variety, 3 different videos were shown each week on a preestablished schedule.

In all 3 conditions, treatment was delivered for 40 minutes each weekday (Monday through Friday) for 8 weeks, after receipt of the daily methadone dose. Patients were instructed to attend treatment daily and were informed of the consequences for nonattendance. No financial incentives were provided for attendance. Treatments were delivered in groups of up to 6 patients, in the same treatment room, and under the same conditions (eg, while recumbent in a reclining chair), but at different times, such that patients in different treatment conditions were not treated together. Patients assigned to the 2 needle-insertion conditions were unaware of whether they were receiving the NADA protocol. All 3 treatment conditions were provided by a professional acupuncturist

(Stephen Birch, PhD) who had more than 10 years' experience as an acupuncturist, acupuncture instructor, and acupuncture scholar, and who was certified to provide the NADA protocol. Patients were informed that the acupuncturist-relaxation trainer was not permitted to engage them in conversation, and patients were instructed not to converse with one another during the session. All sessions were provided with the use of a standardized script, under the observation of a research assistant.

ASSESSMENTS

Urine samples were collected 3 times weekly (Monday, Wednesday, and Friday) while the patient remained in treatment and were tested for the presence of cocaine metabolite (benzoylecognine) using fluorescence polarization immunoassay (TDx; Abbott Laboratories, Abbott Park, Ill), which has been shown to be a reliable and precise assay.²⁷ Samples with benzoylecognine levels of 300 ng/mL or more were considered positive for cocaine. For the range of doses between 13 and 130 mg of topically used cocaine, the test result will remain positive for at least 3 days after cocaine use. This is a clinically reasonable sensitivity for illicit cocaine use by either topical (ie, nasal), freebase, or intravenous routes. The Addiction Severity Index (ASI),²⁸ the Treatment Credibility Scale,²⁹ and the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES Version 8D)³⁰ were administered before treatment (ie, at entry into the trial) and at the end of the 8-week trial (ie, at the 8-week follow-up). The ASI is a structured interview commonly used in addiction research that provides composite scores assessing the severity of 7 addiction-related problem areas. The Treatment Credibility Scale is a 5-item questionnaire that assesses confidence in treatment for the target disorder on scales from 1 (not at all) to 6 (very confident); items were averaged to provide a single treatment credibility score (Cronbach $\alpha = .88$). The SOCRATES is a 19-item questionnaire assessing readiness for substance abuse treatment. Items are rated on scales from 1 (strongly disagree) to 5 (strongly agree), and 3 composite scores are calculated (α values range from .60 to .96). An overall treatment readiness score was calculated by subtracting the "ambivalence" score from the sum of the "problem recognition" and "taking action" scores. A 10-item assessment of therapeutic alliance with the acupuncturist-relaxation trainer, modified from the therapeutic alliance scale,³¹ was administered at the end of the first treatment session and again in weeks 4 and 8. Items were rated on 7-point scales from 1 (never) to 7 (always) and averaged (Cronbach $\alpha = .92$). Acute subjective effects of treatment sessions were assessed weekly on 5-point scales from 0 (not at all) to 4 (extreme), as follows: (1) 5 items assessed pain (ie, pain in ears on needle insertion and pain at needle sites during session) and *de qi*-associated sensations (ie, warmth in ears, activity in ears, and radiating sensations from ears to face, neck, or shoulders); (2) 5 items assessed relaxation effects relative to pre-session levels (eg, relaxed, heaviness, warmth, sleepiness, looser muscles); (3) 5 items assessed satisfaction with the session (eg, session enjoyment, stress reduction, feelings of happiness and peacefulness, and increased confidence in acupuncture as a treatment for cocaine problems); (4) as an additional measure of treatment desirability, participants were asked how much they would be willing to pay for such a treatment session in the future

(nothing, \$5, \$10, \$15, \$20); and (5) as a measure of duration of treatment effects, 1 item, asked the following day, asked how long the previous session's effects lasted (0 indicated no effect; 1, less than 1 hour; 2, 2-3 hours; 3, all afternoon; and 4, all night). As in previous studies,³² items in each category were averaged.

DATA ANALYTIC STRATEGY

The Kaplan-Meier method and log-rank test were used to compare the survival time to dropout. Differential retention by treatment condition on pretreatment sociodemographic and drug use variables, and on perceived treatment credibility, therapeutic alliance, and acute effects of treatment, was examined by means of a series of 3 (treatment condition) \times 2 (retention status) analyses of variance (ANOVAs) on continuous variables and χ^2 analyses by treatment condition and retention status for categorical variables.

Primary treatment outcome analysis was conducted on the intent-to-treat sample. The treatment outcome of primary interest was assessed by 3-times-weekly urine toxicology screens, each of which was coded as a binary response (0, negative; 1, positive). A generalized linear model for longitudinal data was fitted to the data³³ by means of a marginal model. PROC GENMOD in SAS³⁴ was used for the analysis. Baseline urine data (ie, the screening urine test) did not fit smoothly with the observations subsequently taken during treatment and would have required a separate parameter for each treatment condition, thus effectively removing the baseline observations from the tests for treatment effect; therefore, analyses were limited to the thrice-weekly urine screens provided during the course of treatment. The succession of 24 urine toxicology screens constituted the time parameter and were treated as equally spaced.^{33(p75)} Parameters were estimated by means of generalized estimating equations, and the resulting empirical variances were used for statistical inference. Our analytic strategy was first to determine the underlying structure of the correlation between the repeated urine tests by constructing a variogram for the residuals about the proportion that tested positive by treatment condition and time. On the basis of examination of this variogram, which indicated serial correlation among urine test results, an autoregressive, AR(1), covariance structure was used in subsequent analyses. From the unstructured or saturated model, the serial correlation was estimated to be $0.62d$, where d is the difference between urine screen index numbers. Estimates of treatment \times time effects were then used to select an appropriate model or equation that would accurately describe the time trend for each treatment condition. Finally, significance tests of the model were constructed to compare the acupuncture-treated group with each of the 2 control conditions, as well as to obtain an overall test of any differences among the groups. This was accomplished by constructing a Wald test³⁵ for a linear contrast that would address the null hypothesis posed by a particular comparison. The resulting statistics were then compared with a χ^2 distribution with the appropriate degrees of freedom. The empirical covariance of the parameter estimates was used in constructing this test.

Continued on next page

Secondary analyses included analysis of urine data provided by the sample of treatment completers. The number of consecutive cocaine-negative urine samples provided by each treatment completer was calculated, with missed urine samples coded as cocaine positive. These data were entered into ANOVA with planned treatment contrasts. To determine abstinence status at completion of treatment, χ^2 analyses were conducted by treatment condition on percentage of completers who provided 3 consecutive cocaine-negative urine samples during week 8. Change in ASI severity of addiction and SOCRATES motivation scores by treatment condition were also assessed by 3 (group) \times 2 (time) mixed ANOVAs. Data are given as mean \pm SD, unless otherwise indicated.

lated a priori as such, eg, points proximate to active points.^{8,12} However, these points may be too active to be suitable controls.²¹ On the basis of several studies of acute effects conducted by our research group, we provisionally concluded that needles inserted into regions on the helix of the auricle were relatively less active than other potential control needle configurations tested, and therefore would constitute an appropriate control for needle insertion.²¹⁻²³

Herein we report on a randomized clinical trial conducted to determine the efficacy of auricular acupuncture for the treatment of cocaine dependence in methadone-maintained patients with the use of the 2 control procedures previously outlined. This patient population was selected because cocaine use is a serious problem in methadone maintenance programs (MMPs) across the country,²⁴ and thus a community-based MMP provided a pertinent treatment context in which to evaluate auricular acupuncture's efficacy with a relatively difficult-to-treat patient population. The primary outcome for this study was an objective measure of cocaine use based on frequent urine toxicology screens.

RESULTS

PATIENT CHARACTERISTICS

The mean age of the sample was 37 \pm 6 years; 47 (57%) were men and 35 (43%) were women; 36 (44%) were white, 31 (38%) were African American, 13 (16%) were Hispanic, and 2 (2%) identified themselves as "other" minority; 35 (43%) had less than high school education; and 74 (90%) were unemployed. All patients had reached a stable dose of methadone; mean methadone dose during the trial was 78 \pm 17 mg/d.

RETENTION

Eighty-two patients were randomly assigned to a treatment condition and constitute the intent-to-treat sample. Sixty-three percent of these patients completed the 8-week trial; 46% (13/28) completed auricular acupuncture, 63% (17/27) completed the needle-insertion control, and 81%

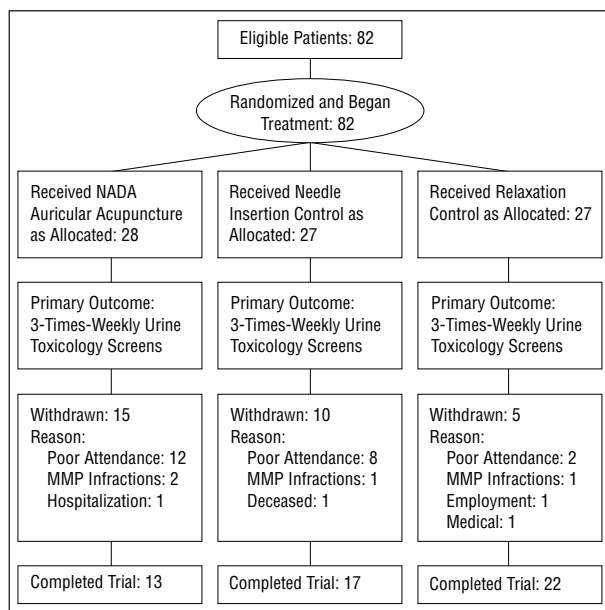


Figure 1. Flow diagram illustrating progress of patients through the trial. NADA indicates National Acupuncture Detoxification Association; MMP, methadone maintenance program.

(22/27) completed the relaxation control. Thus, 52 patients constituted the sample who completed the study. There was a significant difference in survival time in the study (auricular acupuncture, 5.2 \pm 3.0 weeks; needle-insertion control, 6.7 \pm 2.5 weeks; relaxation control, 7.0 \pm 2.3 weeks; log-rank $\chi^2 = 7.84$; $P = .02$). Patients assigned to acupuncture completed significantly fewer treatment weeks than patients assigned to either of the 2 control conditions. There were no significant pretreatment between-group differences on any measured variable, and no significant interactions between retention status and treatment condition. **Table 1** provides a description of the sample by treatment condition and retention status.

PRIMARY ANALYSIS OF INTENT-TO-TREAT SAMPLE: COCAINE USE DURING TREATMENT

There were no pretreatment differences among the treatment conditions on cocaine use during the week before patients entered the trial. For the baseline measurement, 93% (26/28) of the acupuncture group, 100% (27/27) of the needle control group, and 93% (25/27) of the relaxation control group had used cocaine in the week before beginning treatment. The logistic regression parameters for each treatment-time combination for subsequent urine toxicology results during the 8-week trial for the intent-to-treat sample are shown in **Figure 2**. Inspection of the pattern suggested that a break in the line occurred at approximately urine screen 15, and that using a broken line model as a final summary would simplify the observed time pattern and would more accurately characterize the observed trend with time. A formal test suggests that this is indeed the case ($\chi^2 = 0.09$; $P = .95$). The fitted lines for the proportion of cocaine-positive urine tests in each treatment condition are also shown in Figure 2.

The data provide strong evidence for differences among the 3 conditions on the basis of a global test of

Table 1. Summary Statistics of Intent-to-Treat Sample by Treatment Condition and Retention Status*

	Acupuncture (n = 28)		Needle- Insertion Control (n = 27)		Relaxation Control (n = 27)	
	Dropped (n = 15)	Retained (n = 13)	Dropped (n = 10)	Retained (n = 17)	Dropped (n = 5)	Retained (n = 22)
Age, mean ± SD, y	39 ± 7	37 ± 7	36 ± 5	38 ± 5	34 ± 7	38 ± 7
Sex, No. (%) men	8 (53)	8 (61)	7 (70)	8 (47)	1 (20)	15 (68)
Race, No. (%)						
White	8 (53)	6 (46)	5 (50)	9 (53)	2 (40)	6 (27)
African American	4 (27)	4 (31)	4 (40)	6 (35)	1 (20)	12 (54)
Hispanic	3 (20)	3 (23)	1 (10)	2 (12)	1 (20)	3 (14)
Other minority	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	1 (5)
Unemployed, No. (%)	12 (80)	13 (100)	10 (100)	15 (88)	5 (100)	19 (86)
HIV positive, No. (%)	6 (40)	3 (23)	4 (40)	5 (29)	1 (20)	9 (41)
Antisocial personality, No. (%)	2 (13)	0 (0)	5 (50)	2 (12)	0 (0)	2 (9)
Cocaine use, mean ± SD						
Years of use	8 ± 7	9 ± 6	7 ± 8	9 ± 7	4 ± 4	12 ± 7
Bags per week	13 ± 17	5 ± 8	7 ± 5	11 ± 17	3 ± 2	4 ± 4
Days per week	3 ± 3	2 ± 2	4 ± 3	3 ± 2	2 ± 1	3 ± 2
Route of administration, No. (%)						
Intravenous	3 (20)	6 (46)	3 (30)	7 (41)	1 (20)	11 (50)
Smoke	11 (73)	6 (46)	7 (70)	7 (41)	4 (80)	6 (27)
Intranasal	1 (7)	1 (8)	0 (0)	3 (18)	0 (0)	5 (23)
Other, mean ± SD						
Treatment readiness score	44 ± 10	49 ± 9	52 ± 5	50 ± 8	50 ± 7	48 ± 8
ASI score	0.30 ± 0.19	0.28 ± 0.09	0.38 ± 0.11	0.27 ± 0.14	0.28 ± 0.13	0.32 ± 0.13

*There were no significant retention status × treatment condition interactions and no main effects for treatment condition on any of the above variables. HIV indicates human immunodeficiency virus; ASI, Addiction Severity Index.

the null hypothesis that both intercepts and slopes are identical ($\chi^2_4=12.91$; $P=.01$). This is a test of the null hypothesis that the 3 fitted lines in Figure 2 are coincident. Because the trend lines appear to be similar, and a formal test suggested parallel trends ($\chi^2_2=5.29$; $P=.07$), subsequent comparisons among conditions were made by means of a parallel trends model. This approach generally leads to a more powerful test because it is directed at a single parameter instead of 2. The comparison of acupuncture with relaxation was significant ($\chi^2_1=6.54$; $P=.01$), with an estimated overall odds ratio for a cocaine-negative urine screen of 3.41 (95% confidence interval [CI], 1.33-8.72). The comparison of acupuncture with needle control was also significant ($\chi^2_1=3.83$; $P=.05$), with an estimated overall odds ratio for a cocaine-negative urine screen of 2.40 (95% CI, 1.00-5.75). Patients randomly assigned to receive the NADA acupuncture protocol were more likely to provide cocaine-negative urine samples than either the needle-insertion or relaxation controls.

One assumption of the analysis presented above is that data are missing at random in all conditions (ie, the reason an observation was missing was not somehow related to whether an individual previously tested positive for cocaine use). To test this, we examined the relationship between missing data and provision of positive urine screens. The association between whether a test was positive at one visit and missing at the next was analyzed by creating a series of 2×2 tables for each urine screen. The Cochran-Mantel-Haenszel test was not significant for the overall association across screens ($\chi^2_1=0.08$; $P=.77$). Within each condition, the esti-

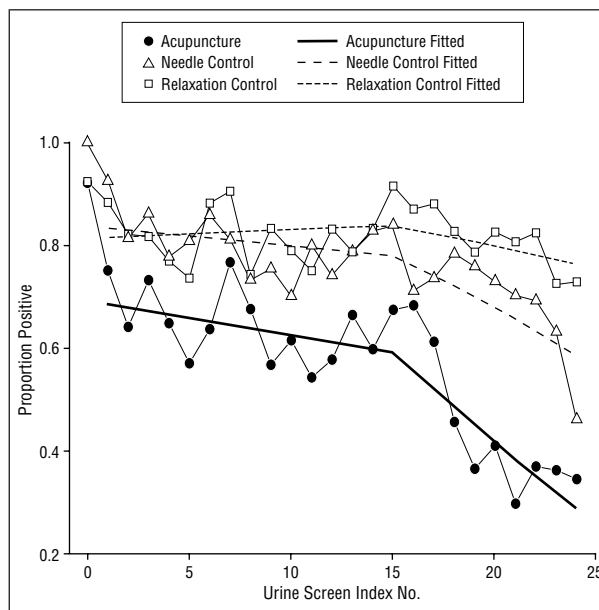


Figure 2. Unstructured and fitted proportions of cocaine-positive urine specimens by time and treatment. Treatment comparisons assume parallel trends. For any treatment difference, $\chi^2_2=7.40$; $P=.03$; acupuncture vs relaxation, $\chi^2_1=6.54$; $P=.01$; acupuncture vs needle insertion, $\chi^2_1=3.83$; $P=.05$.

ated common odds ratios for the association between a positive test result and missing data across screens were 1.55 (95% CI, 0.8-3.1) for acupuncture, 0.8 (95% CI, 0.4-1.5) for the needle control group, and 1.1 (95% CI, 0.5-2.9) for the relaxation control group.

The fact that the acupuncture group had a lower retention rate and therefore provided fewer urine samples than either of the control groups (acupuncture, 15.25 ± 8.12 ; needle control, 19.07 ± 6.19 ; relaxation, 19.96 ± 5.91 ; $F_{2,79} = 3.72$; $P = .03$) also raises the issue of whether the apparent effectiveness of acupuncture was mainly a function of treatment nonresponders differentially dropping out of this condition. To test this, we conducted a 2 (retention status) \times 3 (treatment condition) ANOVA on percentage of urine samples testing positive for cocaine. There was no significant retention \times treatment condition interaction (non-completers: acupuncture, 80.7 ± 32.3 ; needle-insertion control, 89.4 ± 15.3 ; relaxation control, 80.0 ± 34.6 ; completers: acupuncture, 49.5 ± 33.0 ; needle-insertion control, 71.1 ± 33.2 ; relaxation control, 80.5 ± 28.0 ; $F_{2,76} = 1.43$; $P = .25$). Thus, noncompleters were generally comparable across conditions.

SECONDARY ANALYSIS OF OUTCOMES FOR TREATMENT COMPLETERS: CONSECUTIVE COCAINE-NEGATIVE URINE SCREENS AND STATUS AT TREATMENT COMPLETION

Examination of urine data for patients who completed the 8-week trial showed that acupuncture completers provided significantly more consecutive cocaine-negative urine samples than did either the relaxation control group ($P = .002$) or the needle-insertion control group ($P = .02$) (acupuncture, 7.23 ± 6.77 ; needle-insertion control, 3.35 ± 3.55 ; relaxation control, 2.14 ± 3.37 ; $F_{2,49} = 5.37$; $P = .008$). Acupuncture completers were also significantly more likely to provide 3 consecutive cocaine-free urine samples in the final week of the study (acupuncture, 54% [7/13]; needle-insertion control, 24% [4/17]; relaxation control, 9% [2/22]; $\chi^2_2 = 8.76$; $P = .01$).

ADDITIONAL TREATMENT OUTCOMES

There was a main effect for time for severity of drug problems as measured by the ASI, which, collapsed across treatment conditions, decreased significantly from pretreatment to the 8-week follow-up ($F_{1,61} = 5.59$; $P = .02$). There were no other changes in ASI or SOCRATES scores across time and no significant treatment condition \times time interactions.

CHECKS ON INTEGRITY OF THE TREATMENT CONDITIONS

Session Attendance

There was no significant difference among the treatment conditions in average number of sessions attended per week while retained in treatment. For the intent-to-treat sample, the average number of sessions attended per week was as follows: acupuncture, 3.1 ± 1.1 ; needle-insertion control, 3.3 ± 0.8 ; and relaxation control, 3.6 ± 0.6 ($F_{2,79} = 2.05$; $P = .14$). For the completers, average number of sessions attended per week was as follows: acupuncture, 3.6 ± 1.0 ; needle-insertion control, 3.7 ± 0.6 ; relaxation control, 3.7 ± 0.6 ($F_{2,49} = 0.04$; $P = .96$). Thus, session attendance was not greater in the acupunc-

ture treatment condition and was generally comparable across treatment conditions.

Acute Effects of Treatment Sessions

Relaxation controls reported significantly more relaxation effects after sessions than did patients assigned to either type of needle insertion ($F_{2,76} = 6.00$; $P = .004$). There were no significant differences between the 3 treatment conditions in ratings of satisfaction with sessions, duration of treatment effects, or willingness to pay for future sessions. Comparisons between the 2 needle-insertion conditions disclosed no significant differences on ratings of pain or *de qi* sensations.

Treatment Credibility and Therapeutic Alliance

There was no difference by treatment condition on either treatment credibility or therapeutic alliance either at pretreatment or at the 8-week follow-up. There was no significant change in these scores during treatment, nor was there a significant treatment condition \times time interaction. **Table 2** presents mean scores collapsed across time. As shown, patients in each condition found the treatment protocols to be credible and reported a positive therapeutic alliance with the acupuncturist–relaxation trainer.

Relationship Between Acute Response to Treatment Sessions and Treatment Retention

There were no significant differences in any of the previously described measures by retention status, and no significant treatment condition \times retention interactions. Table 2 presents mean (\pm SD) ratings during the 8-week trial by treatment condition and retention status.

COMMENT

Intent-to-treat analysis of longitudinal urine toxicology data indicated that the NADA auricular acupuncture protocol was significantly more effective in reducing cocaine use than either a relaxation control ($P = .01$) or a needle-insertion control ($P = .05$). Analysis of data for treatment completers showed that patients who completed the 8-week course of acupuncture abstained from cocaine significantly longer during treatment and were more likely to be abstinent at completion than either of the control conditions ($P < .05$).

The finding of a positive clinical response to acupuncture is generally consistent with preliminary studies suggesting that the NADA acupuncture protocol shows promise for the treatment of cocaine abuse.^{4,12,36} Failure of previous controlled trials to demonstrate a significant difference between the NADA protocol and a needle-insertion control may have resulted from insufficient differentiation between the active and control conditions. Previous controls have included needle insertion into presumably “inactive” sites proximate to addiction-specific sites, or into “active” sites used for the treatment of other disorders. The needle-insertion control used in the current study—insertion into helix sites—may have provided sufficient differentiation to detect a statistically significant

Table 2. Comparability of Conditions: Subjective Effects of Treatment Sessions, Credibility of Treatment, and Therapeutic Alliance by Treatment Condition and Retention Status*

	Acupuncture (n = 28)		Needle-Insertion Control (n = 27)		Relaxation Control (n = 27)		Group Effect P
	Dropped	Retained	Dropped	Retained	Dropped	Retained	
Relaxation effect	1.5 ± 0.8	1.2 ± 0.6	1.1 ± 0.5	1.3 ± 0.5	1.9 ± 0.4	1.8 ± 0.7	.004†
Satisfaction	1.9 ± 0.8	1.9 ± 0.8	1.8 ± 0.8	1.8 ± 0.5	2.1 ± 0.3	2.1 ± 0.7	.41
Willing to pay	1.8 ± 1.1	1.6 ± 1.0	2.0 ± 1.4	1.5 ± 1.0	1.9 ± 1.3	1.9 ± 1.1	.85
Effect duration	1.7 ± 0.7	1.8 ± 1.0	1.1 ± 0.8	1.9 ± 0.9	1.2 ± 0.6	1.6 ± 0.8	.31
Pain	0.8 ± 0.5	0.6 ± 0.4	0.6 ± 0.5	0.6 ± 0.4	NA	NA	.70
de qi‡	0.6 ± 0.5	0.5 ± 0.4	0.6 ± 0.4	0.5 ± 0.5	NA	NA	.91
Credibility	4.2 ± 1.1	4.4 ± 0.6	4.6 ± 0.9	4.8 ± 1.0	4.5 ± 0.2	4.4 ± 1.2	.34
Alliance	5.5 ± 1.6	5.5 ± 1.3	6.1 ± 1.0	5.7 ± 0.8	4.9 ± 0.6	5.6 ± 0.5	.10

* Values are expressed as mean ± SD. NA indicates not applicable.

† Group main effect for relaxation ($F_{2,76} = 6.00$; $P = .004$); relaxation controls reported significantly more relaxation effects than the acupuncture group ($P = .004$) or needle-insertion controls ($P = .001$). There were no significant treatment condition × retention status interactions.

‡ Warmth in ears, activity in ears, and radiating sensations from ears to face, neck, or shoulders.

difference relative to the active treatment. However, the difference in treatment response between the NADA protocol and the needle-insertion control was smaller than that found between the NADA protocol and the no-needle relaxation control condition, suggesting that future studies enrolling larger samples may be needed to further disentangle possible placebo effects of needle insertion from the therapeutic effectiveness of the NADA protocol.

Placing the current findings within a larger clinical context, the range of effective treatments for cocaine addiction is at present quite limited; thus, if findings from the current study are replicated, acupuncture could be an important addition to current treatment options. Some psychosocial approaches for the treatment of this disorder have been supported by clinical research,³⁷ but no pharmacological agent has demonstrated efficacy in controlled trials. Acupuncture is a treatment modality with a low side-effect profile that does not exclude patients who have difficulty participating in verbally mediated treatment interventions. Also, as in the Lincoln Hospital setting in Bronx, NY, in which the NADA protocol was originally developed,³⁸ it can be provided to large numbers of patients simultaneously, making it a relatively low-cost treatment modality.² Further research investigating cost-effectiveness and predictors of response to acupuncture may be worthwhile.

This study had a number of limitations that should be considered in interpreting our findings. First, the acupuncturist was not blinded with respect to treatment assignment and patients were only partially blinded. Although bias checks suggested that the treatments were equally credible and that therapeutic alliance was comparable across conditions, this does not raise the rigor of this study to the level of one conducted under double-blind conditions. However, procedures, unlike pharmacotherapies, are nearly impossible to evaluate under conditions in which both the patients and the practitioners are blinded. There are several reasons for this. Training and competency are a prerequisite to providing the treatments, and experienced practitioners will therefore know which treatment is hypothesized to be active. In addition, whereas in a pharmacotherapy study the active medication and the pill pla-

cebo can be made identical in appearance, procedures are observably different to all of the participants in the study. Hence, the present study had to be conducted under single-blind conditions. However, several checks against potential bias (eg, observation of the acupuncturist, assessment of therapeutic alliance) were included in the design. Second, participants in this study were dually dependent on cocaine and opiates, were maintained on a regimen of methadone, and had undergone previous unsuccessful treatment attempts provided by their MMP. It is possible that these patients may differ in their response to acupuncture from patients not taking methadone or patients who may be responsive to psychosocial intervention. Therefore, the extent to which our findings are generalizable to other settings or subpopulations is not known. However, it could be argued that a positive treatment response in this difficult-to-treat patient population supports acupuncture's potential generalizability to other substance abuse treatment settings. Finally, the relatively higher dropout rate in the NADA acupuncture condition is unexplained and may have influenced outcome in ways that are not apparent. However, there were no differences in any adverse effects of treatment (eg, pain), and there were no interactions between treatment and retention on any measured patient characteristic, such as severity of addiction or motivation for abstinence, that might influence response to treatment. Furthermore, retention in the NADA acupuncture protocol was also either better than or comparable with that of other studies of pharmacological and psychological treatments for cocaine dependence^{39,40}; thus the relatively low retention rate in the NADA protocol does not weaken its generalizability to other treatment settings.

Because unexplained differential treatment retention is an issue that can potentially obfuscate interpretation of findings from randomized clinical trials, methods for improving retention need to be considered in future studies. Providing incentives to patients to remain in treatment is a strategy that has been used to improve retention in controlled clinical trials; however, this strategy is not without problems,⁴¹ having the potential to alter the treatment being assessed or to produce motivational conflicts.⁴² Various strategies may need to be

considered in future trials of acupuncture to address the problem of differential treatment retention.

The present study also had several strengths. First, the NADA auricular acupuncture protocol was compared with 2 conditions that controlled for multiple nonspecific effects of acupuncture. Comparing a putative active treatment with so-called active placebos constitutes a highly conservative test, one that some pharmacotherapies that are generally regarded as effective have not always passed.⁴³ Second, the randomization procedure was computer based with real-time assignment generated for each patient, which concealed future treatment assignments. Third, the primary outcome variable, cocaine use, was based on a laboratory test of urine screens that were collected 3 times weekly, making it unlikely that instances of cocaine use were missed or that patients could dissemble cocaine abstinence. Fourth, attendance records indicated that, on average, patients in all 3 conditions received a comparable "dose" of the treatments. Finally, evaluators were blinded to patients' treatment assignment.

In conclusion, findings from the present study support the use of acupuncture for the treatment of cocaine addiction. However, these findings should be interpreted relative to the methodological difficulties inherent in evaluating clinical procedures in controlled trials. Further research of acupuncture in this application, including both clinical and foundational studies, appears to be warranted.

Accepted for publication February 28, 2000.

This study was supported by grants DA08513, DA00277, DA09241, and P50-DA09241 from the National Institutes on Drug Abuse, National Institutes of Health, Bethesda, Md.

Acupuncture needles for this study were donated by Seirin Co Ltd, Shimizu-City, Japan.

We thank Stephen Birch, PhD, for contributing his expertise and knowledge regarding acupuncture practice and theory to this project.

Reprints: Arthur Margolin, PhD, Substance Abuse Center, Yale University School of Medicine, 34 Park St, New Haven, CT 06519 (e-mail: arthur.margolin@yale.edu).

REFERENCES

1. Substance Abuse and Mental Health Services Administration. *National Household Survey on Drug Abuse: Population Estimates, 1998*. Washington, DC: Substance Abuse and Mental Health Services Administration; 1999.
2. Brumbaugh AG. *Transformation and Recovery: A Guide for the Design and Development of Acupuncture-Based Chemical Dependence Treatment Programs*. Santa Barbara, Calif: Stillpoint Press; 1995.
3. Culliton P, Kiresuk T. Overview of substance abuse acupuncture treatment research. *J Altern Complement Ther*. 1996;2:149-159.
4. Brewington V, Smith M, Lipton D. Acupuncture as a detoxification treatment: an analysis of controlled research. *J Subst Abuse Treat*. 1994;11:289-307.
5. Gurevich MI, Duckworth D, Imhof JE, Katz JL. Is auricular acupuncture beneficial in the inpatient treatment of substance-abusing patients? *J Subst Abuse Treat*. 1996;13:165-171.
6. Konefal J, Duncan R, Clemence C. The impact of the addition of an acupuncture treatment program to an existing metro-Dade County outpatient substance abuse treatment facility. *J Addict Dis*. 1994;13:71-99.
7. Lipton D, Brewington V, Smith MO. Acupuncture for crack-cocaine detoxification: experimental evaluation of efficacy. *J Subst Abuse Treat*. 1994;11:205-215.
8. Avants SK, Margolin A, Chang P, Kosten TR, Birch S. Acupuncture for the treatment of cocaine addiction: investigation of a needle puncture control. *J Subst Abuse Treat*. 1995;12:195-205.
9. Bullock ML, Kiresuk TJ, Pheley AM, Culliton PD, Lenz SK. Auricular acupuncture in the treatment of cocaine abuse: a study of efficacy and dosing. *J Subst Abuse Treat*. 1999;16:31-38.
10. Otto KC, Quinn C, Sung YF. Auricular acupuncture as an adjunctive treatment for cocaine addiction: a pilot study. *Am J Addict*. 1998;7:164-170.
11. Richard AJ, Montoya ID, Nelson R, Spence RT. Effectiveness of adjunct therapies in crack cocaine treatment. *J Subst Abuse Treat*. 1995;12:401-413.
12. Wells EA, Jackson R, Diaz OR, Stanton V, Saxon AJ, Krupsko A. Acupuncture as an adjunct to methadone treatment services. *Am J Addict*. 1995;4:198-214.
13. Margolin A, Avants SK, Kleber H. Issues investigating complementary therapies in randomized controlled trials. *JAMA*. 1998;280:1626-1628.
14. Vickers A, Cassileth B, Ernst E, et al. How should we research unconventional therapies? a panel report from the Conference on Complementary and Alternative Medicine Research Methodology, National Institutes of Health. *Int J Technol Assess Health Care*. 1997;13:111-121.
15. Lewith GT, Machin D. On the evaluation of the clinical effects of acupuncture. *Pain*. 1983;16:111-127.
16. Vincent CA, Richardson PH. Placebo controls for acupuncture studies. *J R Soc Med*. 1995;88:199-202.
17. Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ*. 1995;311:551-553.
18. Margolin A, Avants SK, Kosten TR. Cue-elicited cocaine craving and autogenic relaxation. *J Subst Abuse Treat*. 1994;11:549-552.
19. Klajner F, Hartman LM, Sobell MB. Treatment of substance abuse by relaxation training: a review of its rationale, efficacy, and mechanisms. *Addict Behav*. 1984;9:41-55.
20. Liao SJ, Lee MHM, Ng LKY. *Principles and Practice of Contemporary Acupuncture*. New York, NY: Marcel Dekker Inc; 1994.
21. Margolin A, Avants SK, Chang P, Birch S, Kosten TR. A single-blind investigation of four auricular needle puncture configurations. *Am J Chin Med*. 1995;23:105-114.
22. Margolin A, Avants SK, Birch S, Falk C, Kleber HD. Methodological investigations for a multisite trial of auricular acupuncture for cocaine addiction: a study of active and control auricular zones. *J Subst Abuse Treat*. 1996;13:471-481.
23. Margolin A, Chang P, Avants SK, Kosten TR. Effects of sham and real auricular needling: implications for trials of acupuncture for cocaine addiction. *Am J Chin Med*. 1993;21:103-111.
24. Condelli WS, Fairbank JA, Dennis ML, Rachal JV. Cocaine use by clients in methadone programs: significance, scope, and behavioral interventions. *J Subst Abuse Treat*. 1992;8:203-212.
25. First M, Spitzer RL, Gibbon M, Williams J. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition (SCID-I/P-Version 2.0)*. New York: Biometrics Research Dept, New York State Psychiatric Institute; 1996.
26. Wei LJ, Lachin JM. Properties of the urn randomization in clinical trials. *Control Clin Trials*. 1988;9:345-364.
27. Poklis A. Evaluation of TDx cocaine metabolite assay. *J Anal Toxicol*. 1987;11:228-230.
28. McLellan AT, Luborsky L, Woody GE, O'Brien CP. An improved diagnostic instrument for substance abuse patients: the Addiction Severity Index. *J Nerv Ment Dis*. 1980;168:26-33.
29. Vincent C. Credibility assessments in trials of acupuncture. *Complement Med Res*. 1990;4:8-11.
30. Miller WR, Tonigan JS. Assessing drinkers' motivation for change: the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES). *Psychol Addict Behav*. 1996;10:81-89.
31. Horvath AO, Greenberg LS. Development and validation of the Working Alliance Inventory. *J Consult Clin Psychol*. 1989;36:223-233.
32. Margolin A, Avants SK. Should cocaine-abusing, buprenorphine-maintained patients receive auricular acupuncture? findings from an acute effects study. *J Altern Complement Med*. 1999;5:567-574.
33. Diggle PJ, Liang K, Zeger SL. *Analysis of Longitudinal Data*. Oxford, England: Clarendon Press; 1994.
34. SAS Institute Inc. *SAS/STAT Software: Changes and Enhancements Through Release 6.12*. Cary, NC: SAS Institute Inc; 1997.
35. Rao CR. *Linear Statistical Inference and Its Applications*. 2nd ed. New York, NY: John Wiley & Sons Inc; 1973.
36. Margolin A, Avants SK, Chang P, Kosten TR. Auricular acupuncture for the treatment of cocaine dependence in methadone-maintained patients. *Am J Addict*. 1992;2:194-200.
37. Carroll KM. Old psychotherapies for cocaine dependence revisited. *Arch Gen Psychiatry*. 1999;56:505-506.
38. Smith MO. Acupuncture treatment for crack: clinical survey of 1,500 patients treated. *Am J Acupuncture*. 1988;16:241-247.
39. Carroll KM, Rounsaville BJ, Gordon LT, et al. Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. *Arch Gen Psychiatry*. 1994;51:177-187.
40. Crits-Christoph P, Siqueland L, Blaine J, et al. Psychosocial treatments for cocaine dependence: National Institute on Drug Abuse Collaborative Cocaine Study. *Arch Gen Psychiatry*. 1999;56:493-502.
41. Lavori PW, Bloch DA, Bridge PT, Leiderman D, LoCastro JS, Somoza E. Plans, designs, and analyses for clinical trials of anti-cocaine medications: where we are today. *J Clin Psychopharmacol*. 1999;19:246-256.
42. Margolin A, Avants SK, Rounsaville B, Kosten TR, Schottenfeld R. Motivational factors in cocaine pharmacotherapy trials with methadone-maintained patients: problems and paradoxes. *J Psychoactive Drugs*. 1997;29:205-212.
43. Fisher S, Greenberg RP. A second opinion: rethinking the claims of biological psychiatry. In: Fisher S, Greenberg RP, eds. *The Limits of Biological Treatments for Psychological Distress*. Hillsdale, NJ: Lawrence A Erlbaum Associates; 1989:309-336.