Acupuncture for posttraumatic stress disorder – A randomized controlled pilot trial

ARTICLE *in* JOURNAL OF NERVOUS & MENTAL DISEASE · JUNE 2007

Impact Factor: 1.81 · DOI: 10.1097/NMD.0b013e31803044f8 · Source: PubMed

4 AUTHORS, INCLUDING:

Michael Hollifield
VA Long Beach Healthcare System
60 PUBLICATIONS **2,009** CITATIONS
SEE PROFILE

Teddy D Warner
University of New Mexico
109 PUBLICATIONS **2,468** CITATIONS
SEE PROFILE

Richard Hammerschlag
Oregon College of Oriental Medicine
102 PUBLICATIONS **1,753** CITATIONS
SEE PROFILE

Acupuncture for Posttraumatic Stress Disorder

A Randomized Controlled Pilot Trial

Michael Hollifield, MD, Nityamo Sinclair-Lian, DOM (NM),† Teddy D. Warner, PhD,† and Richard Hammerschlag, PhD‡*

Abstract: The purpose of the study was to evaluate the potential efficacy and acceptability of acupuncture for posttraumatic stress disorder (PTSD). People diagnosed with PTSD were randomized to either an empirically developed acupuncture treatment (ACU), a group cognitive-behavioral therapy (CBT), or a wait-list control (WLC). The primary outcome measure was self-reported PTSD symptoms at baseline, end treatment, and 3-month follow-up. Repeated measures MANOVA was used to detect predicted Group X Time effects in both intent-to-treat (ITT) and treatment completion models. Compared with the WLC condition in the ITT model, acupuncture provided large treatment effects for PTSD (F [1, 46] = 12.60; $p < 0.01$; Cohen's $d = 1.29$), similar in magnitude to group CBT (F [1, 47] = 12.45; $p < 0.01$; $d = 1.42$) (ACU vs. CBT, $d = 0.29$). Symptom reductions at end treatment were maintained at 3-month follow-up for both interventions. Acupuncture may be an efficacious and acceptable nonexposure treatment option for PTSD. Larger trials with additional controls and methods are warranted to replicate and extend these findings.

Key Words: Acupuncture, clinical trial, cognitive behavioral therapy, oriental medicine, posttraumatic stress disorder, RCT, traditional Chinese medicine.

(*J Nerv Ment Dis* 2007;195: 504–513)

Traditional Chinese medicine (TCM) has been used to treat mental illness since 1100 BC (Hoizey and Hoizey, 1993; Liu, 1981), yet there are no extant clinical or research models in contemporary psychiatry for using acupuncture to treat posttraumatic stress disorder (PTSD). A few preliminary clinical studies utilizing various designs and clinical methods have, however, reported reductions in anxiety. For example, in an open pre/postclinical trial of 18 anxious adults with concomitant insomnia, 10 weekly sessions utilizing clinically indicated acupuncture points significantly diminished state and trait anxiety symptoms, improved sleep, and increased urinary melatonin levels (Spence et al., 2004). A study randomizing 43 subjects with minor depression and 13 subjects with generalized anxiety disorder to either verum acupuncture (classical needle points) or placebo acupuncture demonstrated significant effects on a Clinical Global Impression Score, the Hamilton Anxiety Score, and on clinical response rates for verum but not for placebo acupuncture (Eich et al., 2000). In a study comparing the use of any 2 of 4 acupuncture methods (all provided 30 total sessions in 5 weeks) to a 4-week flexible dose of doxepin HCI for treating anxiety neurosis as defined by the China Criteria for Classification and Diagnosis of Mental Diseases, Hong et al. (2003) found that 72% were either cured or markedly improved in the acupuncture group, which was not significantly different from the 65% in the doxepin group. There is a larger literature of the positive effects of acupuncture for treating depression (Allen et al., 1998; Blitzer et al., 2004; Eich et al., 2000; Han et al., 2004; Luo et al., 1998; Manber et al., 2004; Ng, 1999; Roschke et al., 2000; Schnyer and Allen, 2001; Yang et al., 1994) and insomnia (Montakab, 1999; Phillips and Skelton, 2001; Sok et al., 2003; Spence et al., 2004), two symptoms within diagnostic groups that are highly comorbid with PTSD (Breslau et al., 2000; Krakow et al., 2001; Neria and Bromet, 2000).

The effects of acupuncture are mediated in part by the autonomic nervous system and prefrontal and limbic brain structures, neurological systems that are involved in the pathophysiology of PTSD (Cannistraro and Rauch, 2003; Shen, 2001). The generally sympathoinhibitory effects of acupuncture in animals (Middlekauff et al., 2001) and humans - dependent on needle location and acupuncture type (Haker et al., 2000; Knardahl et al., 1998; Mori et al., 2000; Sugiyama et al., 1995) – may be mediated largely through neurotransmitter systems in an opioid-dependent manner (Chao et al., 1999; Han et al., 1999). The opioid system is hypothesized to be aberrant in anxiety disorders (Sher, 1998). Manual acupuncture causes a broad matrix of central neurological responses involving the amygdala, hippocampus, hypothalamus, cerebellum, basal ganglia, anterior cingulate, insula, and other limbic structures, as seen on functional magnetic resonance imaging (fMRI), positron emission to-

*Department of Psychiatry and Behavioral Sciences and Family and Geriatric Medicine, University of Louisville School of Medicine, Louisville, Kentucky; †Department of Family and Community Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico; and ‡The Oregon College of Oriental Medicine, Portland, Oregon.

Supported by the NIH/National Center for Complementary and Alternative Medicine (NCCAM) No. AT 01229.

Send reprint requests to Michael Hollifield, MD, Department of Psychiatry and Behavioral Sciences, Med Center One, 501 E. Broadway, Louisville, KY 40202.

ISSN: 0022-3018/07/19506-0504
DOI: 10.1097/NMD.0b013e31803044f8

mography (PET) and EEG (reviewed in Napadow et al., 2005). In both animals and humans the response in various CNS targets are dependent on the type of acupuncture and the frequency of stimulation in the case of electroacupuncture (Hui et al., 2000; Kong et al., 2002; Napadow et al., 2005).

This literature provides theoretical reasons to believe that acupuncture may be effective for PTSD. We conducted a pilot study which had 2 aims: (1) to develop a TCM-acupuncture diagnostic and treatment protocol for PTSD, and (2) to evaluate the potential efficacy of acupuncture for treating PTSD in a randomized controlled trial (RCT). The development of the acupuncture protocol is briefly described below and is characterized in detail in a separate report (Sinclair-Lian et al., 2006). Our design to evaluate the potential efficacy of acupuncture for PTSD in this pilot RCT included a no-treatment wait-list group to control for the natural history of PTSD in the recruited population and a standard treatment control for testing relative intervention efficacy.

There are a number of effective interventions for PTSD that could serve as an appropriate standard treatment control. These include cognitive behavioral therapy (CBT) (reviewed in Ehlers et al., 2005), eye movement desensitization and reprocessing (reviewed in Bradley et al., 2005), group imagery rehearsal therapy (Krakow et al., 2001), and various pharmacological therapies as monotherapy or combined with CBT (reviewed in Hollifield et al., 2006). Although trauma-focused CBT produces large treatment effects (Cohen's d = 1.0–1.6) (Ehlers et al., 2005; Foa, 1998; Foa et al., 1999; Resick et al., 2002), it also has limitations, such as nonengagement in treatment and high withdrawal rates (Blanchard et al., 2003; Bryant et al., 2003; Resick et al., 2002; Schnurr et al., 2003; Van Etten and Taylor, 1998), a higher risk of becoming more symptomatic (Tarrier et al., 1999), and the reluctance of many with PTSD to use trauma-focused therapy in clinical practice (Foy et al., 1996; Glynn et al., 1999; Scott and Stradling, 1997). Interventions that minimize exposure to trauma content such as imagery rehearsal therapy (IRT) and stress inoculation training (SIT) are also efficacious for PTSD. A pilot study of IRT in Australian combat veterans and an RCT of group IRT in sexual assault survivors both reported large treatment effects for PTSD symptoms (intent-to-treat d = 0.80 and 1.00, respectively) (Forbes et al., 2003; Krakow et al., 2001). Likewise, SIT has shown large treatment effects for symptoms of PTSD (intent-to-treat d = 0.85) (Foa et al., 1999).

A recent review reported that group interventions for PTSD are efficacious compared with wait list or other "usual care" options (four studies reported a mean standardized mean difference of −0.72 compared with wait list or usual care; Bisson and Andrew, 2005). The largest study of group CBT did not include a nontreatment control group and showed that trauma focused and nontrauma focused group therapy had similar effects on PTSD (Schnurr et al., 2003). Although collective data currently favor individual trauma-focused therapy as more effective, they do not allow definitive conclusions about whether trauma-focused therapy is better than nontrauma focused therapy, or whether individual therapy is better than group therapy for PTSD. In light of these data, an evidence-based group CBT that uses yet minimizes trauma-focus was chosen as the standard treatment control for this pilot trial. Possible limitations of this design and the fact that some standard elements of a definitive trial were appropriately not implemented in this pilot study (e.g., multiple therapists and study sites; use of pre/postclinician-rated interviews; treatment fidelity assessments) are further detailed in the discussion. Our primary hypothesis was that acupuncture would significantly diminish PTSD symptoms with effect sizes larger than a wait-list control and similar in magnitude to that produced by group CBT.

METHODS

Design

This prospective pilot RCT compared the efficacy of an experimental acupuncture treatment to a group CBT treatment control and to a wait-list control (WLC). Individual acupuncture sessions were conducted twice a week for one hour, and group CBT was conducted once a week for 2 hours. Both interventions thus consisted of 24 hours of therapy over 12 weeks with at least 15 min/d of home-based therapy. At 3-month follow-up, maintenance of treatment effects was assessed. Wait-list participants were in contact with the study team only at the assessment periods unless an acute symptom required evaluation, and they were provided either a study treatment by the investigators or were given referrals for treatment at the end of their participation. The study was approved by the Institutional Review Board at the University of New Mexico School of Medicine (UNM), and all participants provided written documentation of informed consent. A data and safety monitoring committee reviewed data management and interim analyses every 3 months during active treatment to ensure data fidelity and participant safety. Participants were enrolled between March 2003 and April 2004. Funding agency personnel had no role in the design, collection, analysis, or interpretation of data, or in writing this report.

Participants, Recruitment, and Randomization

Determination of sample size was predicated on the demonstrated effects of CBT for PTSD, detailed in the introduction. Because we were utilizing group CBT, we predicted a conservative, moderately large effect (i.e., Cohen's d = 0.80), which is on the low end of effect sizes observed in treatment studies for PTSD. With twenty-five participants per group, power is 0.88 to detect a moderately large treatment effect between active and wait-list conditions at alpha of 0.05. A sample of 90 to be randomized to the 3 study groups was planned; 30 per study group to allow for possible withdrawals.

Recruitment was initiated by posting flyers, distributing brochures to clinicians, and by ads in local media. Advertisements defined PTSD and stated that we were recruiting for a nonmedication treatment study for PTSD. Sources of recruitment were posted flyers (43%), other media (29%), UNM clinics and physicians (14%), professional contacts of the research team (5%), participants' word of mouth (4%), community agencies and therapists (2%), and unknown (3%).

A two-stage screening process was used. People with PTSD symptoms and a Posttraumatic Symptom Scale-Self Report (PSS-SR) score of ≥16 were invited for an interview. Eligibility criteria were: (1) DSM-IV diagnosis of PTSD before randomization made by the study principal investigator (M.H.) using the Structured Clinical Interview for DSM-IV (First et al., 2001), (2) a commitment to accept randomization, (3) no active substance abuse or psychosis, and (4) no current active treatment specifically for PTSD. Participants could be in supportive therapy or taking medication for another psychiatric disorder such as depression if the current treatment was stable for ≥3 months and was not anticipated to be changed during the study. Early life trauma, multiple traumatic experiences, or comorbid illness other than psychosis or substance abuse were not exclusions. Traumatic experiences occurred before age 12 in 62% and between age 12 and 17 in 21% of the 84 recruited participants. Thus, 17% of participants experienced trauma only as an adult. Thirty-two (38%) reported experiencing ≥3 events and 28 (33%) identified ≥5 years of ongoing childhood abuse. Those excluded were offered a referral list of treatment sources. All participants were also evaluated by a coinvestigator (N.L.) for TCM diagnosis before randomization to describe TCM diagnoses for PTSD (Sinclair-Lian et al., 2006) and to determine the flexibly prescribed acupuncture points for each participant, further described below in the Interventions section.

Before enrolling participants, 90 study ID numbers were prerandomized to study group (acupuncture, CBT or WLC) by the research coordinator (RC) using a computerized random numbers procedure without restrictions. When a participant was enrolled, the RC opened the assignment program to reveal the participant's group assignment. This allocation procedure was concealed from clinicians. Each enrolled participant was then assigned a treatment ID number by the RC (in sequence of assignation to group), which was used on all documents. The master list linking study ID with treatment ID numbers was kept in a locked file accessible only by the RC, concealed from investigators and clinicians.

Interventions

An important feature of this trial is that it was designed to compare individual acupuncture delivered by one practitioner to group CBT delivered by one other therapist to a wait-list condition. The PI or another physician specializing in PTSD and trained in CBT was on-call at all times for study participants. The study acupuncturist (NL) was also available if a participant receiving acupuncture had questions or concerns.

Acupuncture Treatment

"Acupuncture" is a heterogeneous group of procedures and therapies (Campbell, 1998), and in this study refers to a procedure whereby solid needles were placed into rationally chosen points in subcutaneous tissue or muscle for a given period of time with manipulation. Manual acupuncture (needles without electrical stimulation) was provided by a coinvestigator (NS-L), a licensed Doctor of Oriental Medicine in New Mexico with 4 years postgraduate TCM clinical experience. In TCM clinical practice, regardless of the condition being treated, a practitioner addresses the individual constitution of the patient and plans a series of sessions utilizing unique acupuncture points for each patient. This is similar to a psychiatrist who may diagnose 2 patients with PTSD yet use different interventions for each because of varying clinical characteristics. This practice runs counter to the prevailing scientific methodology involved in designing randomized controlled trials. To satisfy what are considered best practices in TCM as well as scientific methodology, we designed this study to include an intervention with standard acupuncture points for all people diagnosed with PTSD, and with a few flexibly prescribed points that may be added dependent on individual patient characteristics. This design is similar to psychopharmacological studies that allow for a dose range with a minimum dose for all who have the study diagnosis or meet entry criteria. The treatment protocol, discussed in detail in a previous report (Sinclair-Lian et al., 2006), was developed in the first phase of this project by combining information from literature searches, a survey of 20 expert TCM practitioners, and TCM diagnostic information collected from 21 people with PTSD before treatment began.

As shown in Table 1, the standard acupuncture point prescription combined front and back treatments to avoid point fatigue (tolerance due to frequent use). The front treatment used 11 needles, bilateral at acupuncture points LR3, PC6, HT7, ST36, SP6, and 1 at Yintang; the back treatment used 14 needles, bilateral at points GB20, and BL14, 15, 18, 20, 21, and 23. There were 15 other points from which up to 3 flexibly prescribed points could be added to the 25 prescribed needles. Different needling techniques for standard points could also be used to address a participant's specific diagnosis or constitution. Vaccaria seeds, commonly known as "ear seeds," were placed at Shenmen, Sympathetic, Liver, Kidney, and Lung points, and participants were asked to massage the seeds for 15 min/d to help control symptoms. Vaccaria seeds, the size of mustard-seeds, are taped to the ear at specific points for up to a week and are used as a physical adjunct to acupuncture. At the end of treatment, participants were taught how to place the seeds for symptom management.

Individual treatment sessions were conducted for one hour twice per week, and included a standard TCM interview about symptoms (15–20 minutes), pulse and tongue evaluation (2–5 minutes), needle insertion, manipulation, and retention (25–40 minutes), and ear-seed placement (2 minutes). Viva needles, 34 g, were used for most participants and inserted to a depth of ¼ to ½ in. Needles were manipulated at the beginning of treatment and just before needle removal to tonify or reduce the points appropriate to the diagnosis. For needle-sensitive participants, Seirin 40 g (red) was used. Lifestyle advice was limited and given only in response to direct questions by participants or if a behavior was seriously affecting symptoms related to diagnosis and constitution.

Cognitive Behavioral Therapy

The 68-page CBT treatment manual integrates 4 modalities that have direct and theoretical evidence of efficacy

TABLE 1. Traditional Chinese Medicine Diagnoses and Acupuncture Treatment Protocol for PTSD

	Front Points	Back Points
Primary patterns for standard protocol points		
Grounding points/Qi and blood deficiency	ST 36, SP 6	BL 20, BL 21
Primary diagnostic patterns		
Heart Shen disturbances	HT 7, PC 6, Yintang	BL 14, BL 15
Liver Qi stagnation	LR 3, (PC 6)	GB 20, BL 18
Kidney deficiency		BL 23
Secondary patterns for flexibly prescribed points		
Secondary diagnostic patterns		
Liver overacting on spleen	LR 13	(BL 18), (BL 20)
Liver overacting on stomach	LR 14	(BL 18), (BL 21)
Stomach fire	ST 44	GV 14, (BL 21)
Liver fire	LR 2	(GV 14), (BL 18)
Phlegm heat	ST 40	(GV 14), (BL 21)
Phlegm damp	SP 9	(BL 20)
Heart yin/blood deficiency	HT 6	BL 17, (BL 15)
Spleen Qi/Yang deficiency	SP 3	(BL 20), (BL 23)
Kidney Yin/essence deficiency	KI 6	BL 52, (BL 23)
Kidney Yang/Qi deficiency	KI 7	GV 4, (BL 23)
Liver Yin/blood deficiency	LR 8	(BL 17), (BL 18)
Stomach Yin deficiency	(ST 44)	(BL 21)

Parentheses indicate duplicate listing of an acupuncture point.

(reviewed in Bisson and Andrew, 2005; Hobfoll, 1989). Sessions 1 through 3 use psychoeducation, behavioral activation, and activity planning, collectively termed "Trajectory and Resource Loss Stabilization." Participants identify valued resources that have either been lost or are at-risk, and then make plans to engage in activities that will help establish a resource gain cycle. In sessions 4 to 10, participants are taught classic cognitive restructuring (Beck et al., 1979) and imagery rehearsal (Krakow et al., 2001), utilizing material from daily life experiences, much of which is either symbolic or direct trauma content. They are encouraged to also continue behavioral activation and activity planning to regain lost resources. In sessions 10 to 12, participants use classic exposure and desensitization techniques (after Salter, 1949; Wolpe, 1958) while being encouraged to practice earlier session skills. Participants are asked to identify remaining feared or avoided situations, make plans to engage in those situations in the following 6 weeks, and use cognitive restructuring and/or imagery rehearsal as desensitizing reciprocal inhibitors (Wolpe, 1954). All sessions are delivered with a standard approach of agenda setting, education, review of previous sessions and homework, troubleshooting of therapeutic goals and techniques, new technique training, and establishing commitment to engage in at least 15 min/d of homework. Manuals and homework materials are for the participant to use and keep.

Outcome Assessments

Primary and secondary outcomes were assessed by self-report measures at baseline, midtreatment, end treatment, and at one- and three-month follow-up. The RC collected the data, which were concealed from investigator/clinicians. Baseline, end treatment, and 3-month follow-up data are reported.

Primary Outcome

The change in PTSD symptoms on the Posttraumatic Symptom Scale-Self Report (PSS-SR) was the primary outcome measure. The PSS-SR has 17 items that comprise the DSM-IV-TR PTSD diagnostic criteria (Foa et al., 1993). Severity of experiencing each symptom over the past 2 weeks is rated from 0 (not at all) to 3 (very much), and a total severity score is the sum of all items. Scores below 10 are considered mild PTSD, and scores above 20 are severe. The study screening score of $\geq$16 is in the upper moderate range. Cronbach's alpha for internal consistency is adequate (range 0.80–0.91), and one-month test-retest reliability of the overall severity scale is 0.74. Concurrent validity of the PSS-SR for clinical diagnosis has been demonstrated.

Secondary Outcomes

Depression, anxiety, impairment in daily functioning, and satisfaction with care were secondary outcomes. The self-rated Hopkins Symptom Checklist-25 (HSCL-25) (Derogatis et al., 1974; Winokur et al., 1984) was used to assess symptoms of anxiety and depression. The HSCL-25 includes 10 anxiety items and 15 depression items scored on a four-point ordinal severity scale. Scale scores are reported as item averages. The measure has been validated for diagnoses in a general population (Derogatis et al., 1974). The Sheehan Disability Inventory (SDI), used extensively in research, has 3 10-point rating scales that assess impairment in the areas of work, social, and home/family life, and also has

a 5-point global rating scale, which we report here (Sheehan, 1983). Participant satisfaction for those randomized to acupuncture and CBT was assessed at end of treatment using a 10-item rating scale (0 = strongly disagree, 10 = strongly agree), which was developed for this study using expert consensus methods. The satisfaction scale showed good internal consistency ($\alpha = 0.87$) in this population. Retention rates were another measure of treatment satisfaction.

Data Management and Analyses

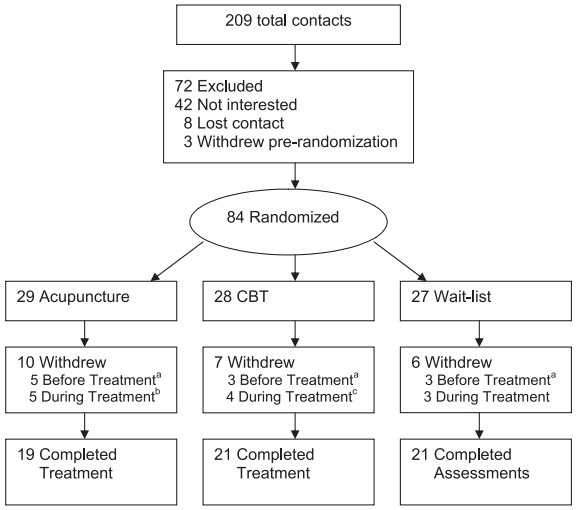
To ensure clinician blinding to outcome data during treatment, the RC was solely responsible for data entry (by study ID number), data verification, and data management. To compare demographic variables by group assignment and treatment status, 9 ethnic groups were collapsed to 4 (white, Hispanic, African American, and Other), age was collapsed to 4 groups (18–25, 26–35, 36–45, and >45), and descriptive and χ^2 statistics were calculated. Repeated measures Group X Time multivariate analysis of variance (MANOVA) was used to compute 3 planned contrasts to compare each pairwise combination of study groups in both intent-to-treat and treatment completion models. This method was chosen over ANCOVA to focus results on actual changes in baseline versus posttreatment symptom levels and to reveal any degree of randomization error of initial symptom levels in this relatively small sample. Within-group treatment effect sizes (i.e., Cohen's *d*; the standardized mean difference), calculated as the change from baseline to end of treatment and from baseline to 3-month follow-up (Cohen, 1987), are reported for each study group.

Due to this being a pilot study with a small sample size, we used common methods for imputing missing data rather than applying complex imputation algorithms (Graham et al., 2003; Rubin, 1996). For the intent-to-treat model, last observation carried forward (LOCF) was used for the 12 participants who withdrew after beginning treatment. This conservative approach was used because there was no evidence that PTSD either improved or deteriorated without further treatment in this sample (the wait-list control group showed no change over 12 weeks). Likewise, LOCF was used to impute follow-up data for all wait-list participants and for the 3 participants who completed treatment but missed the 1 and/or 3-month follow-up assessments. For the 4 participants who completed treatment and missed a single assessment between 2 completed assessments, data were imputed on the slope between the known values.

RESULTS

Recruitment, Sample Demographics, and Treatment Satisfaction

Figure 1 shows the flow of contacts and participant randomization, withdrawal, and completion. Eighty-four participants were randomized, 73 began the protocol, and 61 (73% of those randomized and 84% of those who began the protocol (acupuncture 79% vs. CBT 84% vs. WLC 88%, X^2 [2] = 1.2, $p < 0.56$) completed treatment or wait-list assessments. End treatment and 3-month follow-up assessments were obtained for 60 and 58 participants, respectively.



[a] Individuals who withdrew after randomization but before treatment also were not given baseline assessments and thus cannot be compared on outcomes to those entering or completing treatment.

[b] Reasons for withdrawal from acupuncture treatment:

1 incarcerated
2 conflicting medical treatment (1 had arm surgery and 1 developed prostate cancer)
1 perceived adverse effects from acupuncture (kidney pain)
1 could not keep appointment schedule – 3 no-shows

[c] Reasons for withdrawal from CBT treatment:

2 without reason given
2 could not keep appointment schedule

FIGURE 1. Flow of participants.

Trial completers showed no reliable differences compared with trial noncompleters on any demographic variables or on any of the clinical outcome variables at baseline. Reasons for withdrawal from treatment are listed at the end of Figure 1.

Table 2 shows that there were no reliable differences between assigned groups by gender, age, marital status or education. There were, however, statistically significant differences between assigned groups by ethnicity (X^2 [6] = 14.65, $p = 0.02$).

Primary Outcome: PTSD Symptoms

Intent-to-Treat Model

Repeated measures MANOVA's (Time [Baseline vs. End-Treatment] X Group [Acupuncture or CBT vs. WLC]) (Table 3) showed the predicted contrasts for the Time X Group interaction effect for Acupuncture versus WLC (F [1, 46] = 12.60, $p < 0.01$) and for CBT versus WLC (F [1, 47] = 12.45, $p < 0.01$). A third contrast comparing Acupuncture to CBT revealed the predicted absence of a Time X Group interaction (F [1, 47] = 1.16, $p = 0.29$), indicating no reliable treatment difference for Acupuncture versus CBT. Shown in Figure 2, simple effects analyses showed that PSS-SR scores declined significantly from baseline to end treatment of both the Acupuncture group ($n = 24$, means = 31.3 [10.1] vs. 15.7 [14.0], $p < 0.01$, Cohen's $d = 1.29$) and the CBT group ($n = 25$, means = 32.5 [6.6] vs. 20.0 [10.6], $p < 0.01$, $d = 1.42$)

TABLE 2. Participant Characteristics by Group

Characteristic	Acupuncture (*N* = 29)	CBT (*N* = 28)	Wait-List (*N* = 27)
Mean Age (SD)	42.3 (12.1)	40.9 (13.4)	43.4 (13.5)
Gender			
Male	11	6	10
Female	18	22	17
Ethnicity*			
Caucasian-non-Hispanic	15	26	13
Caucasian-Hispanic	9	2	10
African American	2	0	1
Other	2	0	2
Marital status			
Single	13	10	13
Married	4	7	4
Divorced	10	10	6
Widowed	0	1	3
Education			
<High school	0	0	1
High school diploma or GED	11	8	5
Associates or bachelors degree	12	10	12
MA/PhD/professional	5	10	8

Missing data: $n = 2$ for ethnicity; $n = 3$ for marital status; $n = 2$ for education status.
*Group difference for ethnicity; X^2 (6) = 14.65; $p = 0.02$.

but not for the WLC group ($n = 24$, means = 30.8 [9.5] vs. 27.9 [12.3], *NS*, $d = 0.26$). Not shown in the table, 63% (15 of 24 people) in the Acupuncture group, 36% (9 of 25 people) in the CBT group, and 17% (4 of 24 people) in the WLC group had PSS-SR scores below the entry criterion level of ≥16 at end treatment.

Similar parallel contrasts showed that the reduction of PTSD symptoms for those who received either Acupuncture or CBT was maintained at the 3-month follow-up assessment. PSS-SR scores at 3-months were 15.4 [12.5] ($p < 0.01$, $d = 1.40$ baseline to 3-month) for the Acupuncture group, and 16.7 [12.2] ($p < 0.01$, $d = 1.61$) for the CBT group. At 3 months, 63% ($n = 15$) in the Acupuncture group were below the entry criterion score of ≥16, whereas 52% ($n = 13$) in the CBT group were below the entry criterion score.

Treatment Completion Model

As before, repeated measures MANOVA (Time [Baseline vs. End-Treatment] X Group [Acupuncture or CBT vs. WLC]) showed the predicted contrasts for the Time X Group interaction effect for Acupuncture versus WLC (F [1, 38] = 17.45, $p < 0.01$) and for CBT versus WLC (F [1, 40] = 20.97, $p < 0.01$). A third repeated measures contrast that compared Acupuncture to CBT revealed the absence of a Time X Group interaction (F [1, 38] = 0.84, $p = 0.37$), again indicating that the treatment effects for Acupuncture and CBT were not reliably different. Thus, results for the intent-to-treat and completer models are consistent. Simple effects analyses for those who completed treatment also showed a significant reduction of PSS-SR scores from baseline to end treatment of both the Acupuncture group ($n = 19$, means = 31.3 [8.4] vs. 14.3 [12.1], $p < 0.01$, $d = 1.63$) and the CBT group ($n = 21$, means = 32.0 [6.4] vs. 17.5 [8.3], $p < 0.01$, $d = 1.95$) but not for the WLC group ($n = 21$, means = 29.1 [8.9] vs. 27.5 [12.5], *NS*, $d = 0.15$). By the end of treatment, 68% (13 of 19 people) in the Acupuncture group, 43% (9 of 21 people) in the CBT group, and 19% (4 of 21 people) in the WLC group had PSS-SR scores below the entry criterion level of ≥16.

Parallel contrasts also showed that the reduction of PTSD symptoms for those who completed treatment with either Acupuncture or CBT were maintained at the 3-month follow-up assessment (PSS-SR scores of 14.0 [9.9], $p < 0.01$, $d = 1.88$ baseline to 3-month for the acupuncture group, and 13.5 [9.5], $p < 0.01$, $d = 2.28$ for the CBT group). At 3-months, 68% ($n = 13$) in the Acupuncture group remained below the entry criterion score of ≥16, whereas 62% ($n = 13$) in the CBT group were below the entry criterion score.

Secondary Outcomes: Depression, Anxiety, Impairment, and Satisfaction With Care

Treatment effects for depression, anxiety, and impairment were similar to effects for PTSD, and both treatment groups improved significantly more than the WLC group in both the intent-to-treat (ITT) and the treatment completion model. In the ITT model, shown in Table 3, the Group X Time contrast from baseline to end treatment was significant for comparing Acupuncture versus WLC for depression (*d's* = 0.83 vs. 0.12, respectively, $p < 0.01$), anxiety (*d's* = 1.28 vs. 0.19, $p < 0.01$), and global impairment scores (*d's* = 0.75 vs. 0.04, $p = 0.01$), as well as for comparing CBT versus WLC for depression (*d's* = 1.08 vs. 0.12, $p < 0.01$), anxiety (*d's* = 1.28 vs. 0.19, $p < 0.01$), and global impairment scores (*d's* = 0.76 vs. 0.04, $p < 0.01$). As with PTSD, the contrast of Acupuncture to CBT was not significant for any of these secondary outcomes, indicating similar effects for acupuncture and CBT on all secondary outcomes in the ITT model. Also as with PTSD, contrasts of end treatment means to 3-month follow-up means showed that improvements in depression, anxiety, and global impairment were maintained for both Acupuncture and CBT treatment groups. Thus, simple effects analyses for the secondary outcomes in the ITT model show that treatment group (but not WLC) effect sizes were large from baseline to end treatment and that these treatment effects were maintained 3 months after the end of treatment.

Acupuncture and CBT patients expressed the same level of satisfaction with care on 7 of the 10 items, including the global satisfaction with care item (acupuncture mean rating = 9.2 vs. CBT 9.7 on a 0 to 10 scale where 10 is highest satisfaction, $p = 0.11$). Participants in the acupuncture group compared with the CBT group more strongly agreed that they felt good about doing what they were supposed to do between treatment sessions (means = 9.20 vs. 8.38, F [1, 39] = 4.31, $p = 0.04$). Participants in the CBT group more strongly agreed that they understood the reason for the treatment they received (means = 9.90 vs. 9.15, F [1, 39] = 7.03, $p = 0.01$), and more strongly agreed that their treating clinician helped them understand why the treat-

TABLE 3. Treatment Effects on All Outcomes Using an *Intent-to-Treat Model*

Measure	Group	Baseline Mean (*SD*)	End-Treatment Mean (*SD*)	3-mo Follow-up Mean (*SD*)	Cohen's *d* Baseline End-Treat	Cohen's *d* Baseline 3 mo
PTSD (PSS-SR)	ACU ($n = 24$)	31.33 (10.10)	15.65 (13.95)	15.42 (12.54)	1.29*	1.40*
	CBT ($n = 25$)	32.52 (6.63)	20.02 (10.56)	16.68 (12.20)	1.42*	1.61*
	WLC ($n = 24$)	30.79 (9.54)	27.92 (12.33)	27.92 (12.33)	0.26	0.26
Depression (HSCL-25)	ACU ($n = 24$)	2.50 (0.70)	1.89 (0.76)	1.88 (0.75)	0.83*	0.85*
	CBT ($n = 25$)	2.63 (0.53)	2.00 (0.63)	1.91 (0.69)	1.08*	1.17*
	WLC ($n = 24$)	2.61 (0.65)	2.53 (0.67)	2.53 (0.67)	0.12	0.12
Anxiety (HSCL-25)	ACU ($n = 24$)	2.45 (0.57)	1.67 (0.72)	1.66 (0.56)	1.28*	1.40*
	CBT ($n = 25$)	2.40 (0.42)	1.78 (0.54)	1.81 (0.61)	1.28*	1.13*
	WLC ($n = 24$)	2.26 (0.67)	2.14 (0.61)	2.14 (0.61)	0.19	0.19
Impairment (Sheehan)	ACU ($n = 24$)	3.78 (0.83)	2.98 (1.26)	2.79 (1.32)	0.75*	0.90*
	CBT ($n = 25$)	4.09 (0.81)	3.30 (1.22)	3.00 (1.29)	0.76*	1.01*
	WLC ($n = 24$)	4.00 (1.02)	3.96 (1.04)	3.96 (1.04)	0.04	0.04

Pairwise contrasts from a Group by Time (baseline to end of treatment) repeated measures MANOVA for:

Posttraumatic Stress Disorder (PTSD):

(1) ACU vs. CBT model: $F(1, 47) = 1.16$; $p = 0.29$.
(2) ACU vs. WLC model: $F(1, 46) = 12.60$; $p < 0.01$.
(3) CBT vs. WLC model: $F(1, 47) = 12.45$; $p < 0.01$.

Depression:

(1) ACU vs. CBT model: $F(1, 47) = 0.08$; $p = 0.77$.
(2) ACU vs. WLC model: $F(1, 46) = 8.95$; $p < 0.01$.
(3) CBT vs. WLC model: $F(1, 47) = 10.84$; $p < 0.01$.

Anxiety:

(1) ACU vs. CBT model: $F(1, 47) = 1.09$; $p = 0.30$.
(2) ACU vs. WLC model: $F(1, 46) = 19.43$; $p < 0.01$.
(3) CBT vs. WLC model: $F(1, 47) = 13.30$; $p < 0.01$.

Impairment:

(1) ACU vs. CBT model: $F(1, 43) = 0.05$; $p = 0.83$.
(2) ACU vs. WLC model: $F(1, 43) = 7.28$; $p = 0.01$.
(3) CBT vs. WLC model: $F(1, 44) = 7.76$; $p < 0.01$.

ACU, Acupuncture; CBT, Cognitive Behavioral Therapy; WLC, Wait List Control.
*Univariate simple effect contrasts for time within group are significant at $p < 0.05$.

ment they received might be helpful (means = 9.76 vs. 8.60, $F[1, 39] = 8.62$, $p < 0.01$). However, both groups expressed high satisfaction on all 10 items.

DISCUSSION

This randomized controlled pilot trial indicates that acupuncture may be efficacious for reducing symptoms of PTSD, depression, anxiety, and impairment in people diagnosed with DSM-IV PTSD. Acupuncture provided treatment effects similar to a group CBT intervention, and both interventions were superior to a wait-list control condition for all outcome measures. Furthermore, treatment effects of both acupuncture and group CBT were maintained for 3 months after the end of treatment. Although the percentage of people who fell below the entry criterion score of ≥16 on the PSS-SR after treatment and follow-up was 63% for acupuncture and 52% for CBT in an intent-to-treat model, another 10% in each intervention group scored between 17 and 20, which is in the "moderate" symptom range. In addition, acupuncture and group CBT were equally acceptable to participants for treating PTSD, although our limited sample size does not allow inferences about participant characteristics that might predict continuation or withdrawal with either acupuncture or group CBT. The type of research design used in this study, which compares real-world treatment options, has considerable potential for informing clinical decision making. Unlike placebo-controlled designs, so-called positive controls (Temple, 1989), active control equivalence trials (Makuch and Johanson, 1989) or non-inferiority trials (Pigeot et al., 2003) permit direct comparisons of treatment efficacy.

Limitations of this study are consistent with the early-phase nature of the trial. Each intervention was one approach delivered by one practitioner. The protocols were, however, designed to provide similarities for nonspecific factors by having 24 hours of total in-treatment time and ≥15 min/d of prescribed home care (ear seeds for acupuncture and homework for CBT). Although both interventions provided large effects on all outcomes compared with a wait-list condition, it is possible that these effects were all or partly due to nonspecific therapist factors. A future larger study with multiple therapists and a placebo control group may help discriminate specific from nonspecific effects. Due to constraints of a pilot study, monitoring of therapist adherence to treatment protocols was not conducted nor were outcomes assessed with clinician-rated interviews. However, both treat-

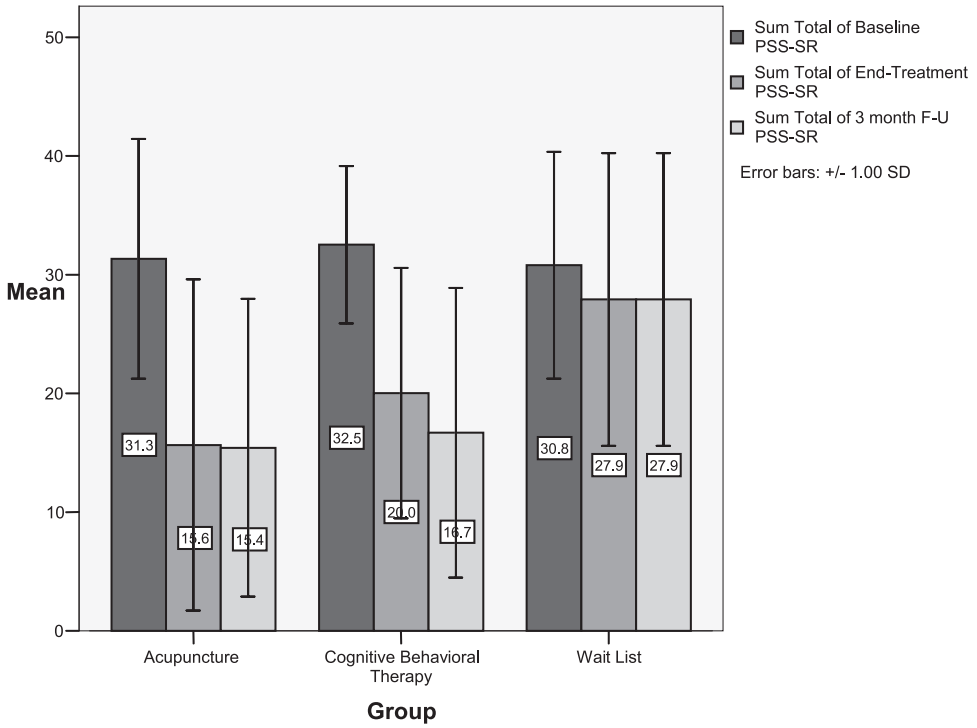


FIGURE 2. Posttraumatic Stress Symptom Score (PSS-SR), Group X Time, Intent to Treat.

ments were delivered with a structured protocol and treatment manual. A larger study with multiple clinicians and treatment monitoring will be needed to determine if there are operator-dependent effects.

The participants in this study were relatively highly educated treatment-seekers who responded to advertisements for a nonmedication study, so they may have been psychologically primed and motivated for improvement using either therapy. These population characteristics likely limit the generalizability of these findings, such that less motivated PTSD sufferers may not fare as well. However, population characteristics alone would not explain the essential equivalence of acupuncture to group CBT and the superiority of both active treatments to a wait-list condition.

The research coordinator collected, entered, and helped analyze the data. Although he was aware of participant group allocation at the time he collected data, he did not assist participants in completing the self-rated assessments. It is possible, yet we think quite unlikely, that he could have systematically influenced participant reports.

We obtained a commitment from participants to not engage in or alter other stable concurrent treatment unless it was allowable by study protocol. We verbally assessed adherence to this commitment throughout the study. However, we did not otherwise objectively monitor concurrent treatment, so specific conclusions about possible concurrent treatment effects cannot be drawn. This will be important to assess in a larger RCT.

Another possible limitation is that the specific group CBT used in this study has not been evaluated in previous research, which, coupled with the fact that a single therapist for each intervention was used, limits interpretation of the relative efficacy of acupuncture to CBT as a whole. We do not know how the group CBT in this study would compare with other group or individual CBT interventions. Similarly, there are no data comparing this group CBT to other proven therapies for PTSD, such as pharmacotherapy, imagery rehearsal therapy alone, stress inoculation training, or eye movement desensitization and reprocessing. If any of these interventions were to be found superior to the group CBT used in this study, then the relative efficacy of acupuncture may be found to be less than current standard treatment. Although our CBT approach was novel in its sequencing of elements, it used evidence-based modalities including classical cognitive restructuring, imagery rehearsal, and significant exposure and desensitization to traumatic content.

Furthermore, the treatment effect size for the group CBT in this study in an intent-to-treat model was within or just above the range of 1.0 to 1.6 reported in most other studies of individual CBT treatment of PTSD (Van Etten and Taylor, 1998). This provides support for the present group CBT model as an adequate standard treatment control and lends further support for the efficacy of group CBT for PTSD. A recent report showed that individual cognitive therapy provided very large effects (d = 2.7–2.8) for PTSD. However, people who could not attribute their current PTSD to discrete traumatic events in adulthood and those with borderline personality disorder were excluded (Ehlers et al., 2005). Half of their participants had experienced earlier traumatic events. In our study, 83% of the participants were traumatized before age 18, one-third had experienced recurrent childhood abuse, making the "traumatic source" of their PTSD uncer-

tain, and we did not assess for or exclude borderline personality disorder. Differences in participant characteristics may help explain differences in therapeutic effects.

In spite of the limitations to this pilot study, the data provide initial evidence that an acupuncture treatment approach may be effective and acceptable for treating PTSD. This interpretation needs to be viewed with cautious optimism, and acupuncture should not be recommended as a treatment of PTSD unless further corroborative and more definitive data become available. This is the first acupuncture protocol that we know of that has been empirically developed and studied for the treatment of PTSD. This study was not designed to evaluate possible mechanisms of action of acupuncture, changes in physiology with treatment, or to compare different acupuncture treatment styles or points for treating PTSD. Treatment effects may be largely due to nonspecific effects of this style of acupuncture that was provided by one practitioner. There is a debate about what comprises optimal acupuncture treatment in general, and whether traditional points in the context of TCM practice are the optimal administration. For example, electro-acupuncture may be more effective than manual acupuncture for treating pain syndromes (Tsui and Leung, 2002; Ulett et al., 1998; Yang et al., 1994). Conducting polymer pads may be as effective as electro-acupuncture for releasing brain neuropeptides (Wang et al., 1992). These results at least suggest that acupuncture may potentially be a new approach for treating PTSD, and provides the basis for a multisite replication trial with additional control groups, multiple therapists, treatment validation procedures, and blinded outcome assessment.

ACKNOWLEDGMENTS

Data were collected while Dr. Hollifield was faculty at the University of New Mexico School of Medicine, Albuquerque, New Mexico. We appreciate the expert consultation of XuiJuan Yang, MD, PhD and Jenna Viscaya, DOM (NM), the assistance of James Ruiz, Marjorie Pilkinton, and Shraddha Singh, PhD, and the contributions of Kathryn Kaminsky, RN, Gerardo Villarreal, MD, and Cosette Wheeler, PhD.

REFERENCES

Allen JJB, Schnyer RN, Hitt SK (1998) The efficacy of acupuncture in the treatment of major depression in women. *Psychol Sci*. 9:397–401.

Beck AT, Rush AJ, Shaw BF (1979) *Cognitive Therapy of Depression.* New York: Guilford.

Bisson J, Andrew M (2005) Psychological treatment of post-traumatic stress disorder (PTSD). *Cochrane Database Syst Rev*. (2):CD003388.

Blanchard EB, Hickling EJ, Devineni T, Veazey CH, Galovski TE, Mundy E, Malta LS, Buckley TC (2003) A controlled evaluation of cognitive behavioural therapy for posttraumatic stress in motor vehicle accident survivors. *Behav Res Ther*. 41:79–86.

Blitzer L, Atchinson-Nevel D, Kenny M (2004) Using acupuncture to treat major depressive disorder: A pilot investigation. *Clin Acupunct Oriental Med*. 4:144–147.

Bradley R, Greene J, Russ E, Dutra L, Westen D (2005) A multidimensional meta-analysis of psychotherapy for PTSD. *Am J Psychiatry*. 162:214–227.

Breslau ND, Davis GC, Peterson EL, Schultz LR (2000) A second look at comorbidity in victims of trauma: The posttraumatic stress disorder-major depression connection. *Biol Psychiatry*. 48:902–909.

Bryant RA, Moulds ML, Guthrie RM, Dang ST, Nixon RDV (2003) Imaginal exposure alone and imaginal exposure with cognitive restructuring in treatment of posttraumatic stress disorder. *J Consult Clin Psychol*. 71:706–712.

Campbell P (1998) Alternative therapies resources. *J Emerg Nurs*. 24:600.

Cannistraro PA, Rauch SL (2003) Neural circuitry of anxiety: Evidence from structural and functional neuroimaging studies. *Psychopharmacol Bull*. 37:8–25.

Chao DM, Shen LL, Tjen ALS, Pitsillides KF, Li P, Longhurst JC (1999) Naloxone reverses inhibitory effect of electroacupuncture on sympathetic cardiovascular reflex responses. *Am J Physiol*. 276:H2127–H2134.

Cohen J (1987) *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale (NJ): Erlbaum.

Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L (1974) The Hopkins Symptom Checklist (HSCL): A measure of primary symptom dimensions. In P Basel (Ed), *Modern Problems in Pharmacopsychiatry*. Basel, Switzerland: Karger.

Ehlers A, Clark DM, Hackmann A, McManus F, Fennel M (2005) Cognitive therapy for post-traumatic stress disorder: Development and evaluation. *Behav Res Ther*. 43:413–431.

Eich H, Agelink MW, Lehmann E, Lemmer W, Klieser E (2000) Acupuncture in patients with minor depression or generalized anxiety disorders: Results of a randomized study. *Fortsch Neurol Psychiatrie*. 68:137–144.

First MB, Spitzer RL, Gibbon M, Williams JBW (2001) *Clinical Interview for DSM-IV Axis I Disorders.* Washington (DC): American Psychiatric Press.

Foa EB (1998) New developments in the treatment of PTSD. In *Annual Meeting of the American Association of Behavioral Therapist.* Washington DC.

Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows EA, Street GP (1999) A comparison of exposure therapy, stress inoculation training and their combination for reducing posttraumatic stress disorder in female assault victims. *J Consult Clin Psychol*. 67:194–200.

Foa EB, Riggs DS, Dancu CV, Rothbaum BO (1993) Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. *J Trauma Stress*. 6:459–473.

Forbes D, Phelps AJ, McHugh AF, Debenham P, Hopwood M, Creamer M (2003) Imagery rehearsal in the treatment of posttraumatic nightmares in Australian veterans with chronic combat-related PTSD: 12-month follow-up data. *J Trauma Stress*. 16:509–513.

Foy DW, Kagan B, McDermott C, Leskin G, Sipprelle RC, Paz GG (1996) Practical parameters in the use of flooding for treating chronic PTSD. *Clin Psychol Psychother*. 3:169–175.

Glynn SM, Eth S, Randolph ET, Foy DW, Urbaitis M, Boxer L, Paz GG, Leong GB, Firman G, Salk JD, Katzman JW, Crothers J (1999) A test of behavioral family therapy to augment exposure for combat-related posttraumatic stress disorder. *J Consult Clin Psychol*. 67:243–251.

Graham JW, Cumsille PE, Elek-Fisk E (2003) Methods for handling missing data. In JA Schinka, WF Velicer (Eds), *Comprehenisve Handbook of Psychology, Vol 2: Research Methods in Psychology*. New York: Wiley.

Haker E, Egekvist H, Bjerring P (2000) Effect of sensory stimulation (acupuncture) on sympathetic and parasympathetic activities in healthy subjects. *J Auton Nerv Syst*. 79:52–59.

Han C, Li X, Luo H, Zhao X, Li X (2004) Clinical study on electro-acupuncture treatment for 30 cases of mental depression. *J Tradit Chin Med*. 24:172–176.

Han SH, Yoon SH, Cho YW, Kim CJ, Min BI (1999) Inhibitory effects of electroacupuncture on stress responses evoked by tooth-pulp stimulation in rats. *Physiol Behav*. 66:217–222.

Hobfoll SE (1989) Conservation of resources. A new attempt at conceptualizing stress. *Am Psychol*. 44:13–24.

Hoizey D, Hoizey M-J (1993) *A History of Chinese Medicine.* Translation by P. Bailey. Edinburgh: Edinburgh University Press.

Hollifield M, Mackey A, Davidson J (2006) Integrating Therapies for Anxiety Disorders. *Psychiatr Ann*. 35:329–338.

Hong Z, Zheng Z, Hong D (2003) Acupuncture treatment for 157 cases of anxiety neurosis. *J Tradit Chin Med*. 23:55–56.

Hui KK, Liu J, Makris N, Gollub RL, Chen AJ, Moore CI, Kennedy DN, Rosen BR (2000) Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Hum Brain Mapp*. 9:13–25.

Knardahl S, Elam M, Olausson B, Wallin BG (1998) Sympathetic nerve activity after acupuncture in humans. *Pain*. 75:19–25.

Kong JN, Ma L, Gollub RL, Wei J, Yang X, Li D, Weng H, Jia F, Wang C, Li F, Li R, Zhuang D (2002) A pilot study of functional magnetic resonance imaging of the brain during manual and electroacupuncture stimulation of acupuncture point (LI-4 Hegu) in normal subjects reveals differential brain activation between methods. *J Altern Complement Med*. 8:411–419.

Krakow B, Hollifield M, Johnston L, Koss M, Schrader R, Warner T, Tandberg D, Lauriello J, McBride L, Cutchen L, Cheng D, Emmons S, Germain A, Melendrez D, Sandoval D, Prince H (2001) Imagery Rehearsal Therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder. A randomized controlled trial. *JAMA*. 286: 537–545.

Liu X (1981) Psychiatry in Traditional Chinese Medicine. *Br J Psychiatry*. 138:429–433.

Luo H, Meng F, Jia Y, Zhao X (1998) Clinical research on the therapeutic effect of the electro-acupuncture treatment in patients with depression. *Psychiatry Clin Neurosci*. 52:S338–S340.

Makuch R, Johnson M (1989) Issues in planning and interpreting active control equivalence studies. *J Clin Epidemiol*. 42:503–511.

Manber R, Schnyer RN, Allen JJ, Rush AJ, Blasey CM (2004) Acupuncture: a promising treatment for depression during pregnancy. *J Affect Disord*. 83:89–95.

Middlekauff HR, Yu JL, Hui K (2001) Acupuncture effects on reflex responses to mental stress in humans. *Am J Physiol Regulatory Integr Compar Physiol*. 280:R1462–R1468.

Montakab H (1999) [Acupuncture and insomnia]. *Forsch Komplementarmed*. 6:29–31.

Mori H, Uchida S, Ohsawa H, Noguchi E, Kimura T, Nishijo K (2000) Electro-acupuncture stimulation to a hindpaw and a hind leg produces different reflex responses in sympathoadrenal medullary function in anesthetized rats. *J Auton Nerv Syst*. 79:93–98.

Napadow V, Makris N, Liu J, Kettner NW, Kwong KK, Hui KK (2005) Effects of electroacupuncture versus manual acupuncture on the human brain as measured by MRI. *Hum Brain Mapp*. 24:193–205.

Neria Y, Bromet EJ (2000) Comorbidity of PTSD and depression: linked or separate incidence. *Biol Psychiatry*. 48:878–880.

Ng M (1999) The effectiveness of traditional Chinese medicine on depressive symptoms. *Diss Abstr Int B Sci Eng*. 60:0860.

Phillips KD, Skelton WD (2001) Effects of individualized acupuncture on sleep quality in HIV disease. *J Assoc Nurses AIDS Care*. 12:27–39.

Pigeot I, Schafer J, Rohmel J, Hauschke D (2003) Assessing non-inferiority of a new treatment in a three-arm clinical trial including a placebo. *Stat Med*. 22:883–899.

Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA (2002) A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. *J Consult Clin Psychol*. 70:867–879.

Roschke J, Wolf C, Muller MJ, Wagner P, Mann K, Grozinger M, Bech S (2000) The benefit from whole body acupuncture in major depression. *J Affect Disord*. 57:73–81.

Rubin D (1996) Multiple imputation after 18+ years. *J Am Stat Assoc*. 91:473–489.

Salter A (1949) *Conditioned Reflex Therapy*. New York: Creative Age.

Schnurr PP, Lunney CA, Sengupta A, Waelde LC (2003) A descriptive analysis of PTSD chronicity in Vietnam veterans. *J Trauma Stress*. 16:545–553.

Schnyer R, Allen JJ (2001) *Acupuncture in the Treatment of Depression: A Manual for Practice and Research*. London: Churchill-Livingston.

Scott MJ, Stradling SG (1997) Client compliance with exposure treatments for posttraumatic stress disorder. *J Trauma Stress*. 10:523–526.

Sheehan D (1983) *The Anxiety Disease*. New York: Scribner.

Shen J (2001) Research on the neurophysiological mechanisms of acupuncture: Review of selected studies and methodological issues. *J Altern Complement Med*. 7:S121–S127.

Sher L (1998) The role of the endogenous opioid system in the pathogenesis of anxiety disorders. *Med Hypoth*. 50:473–474.

Sinclair-Lian N, Hollifield M, Menache M, Warner TD, Viscaya J, Hammerschlag R (2006) Developing traditional Chinese medicine diagnostic structure for posttraumatic stress disorder. *J Altern Complement Med*. 12:45–57.

Sok SR, Erlen JA, Kim KB (2003) Effects of acupuncture therapy on insomnia. *J Adv Nurs*. 44:375–384.

Spence DW, Kayumov L, Chen A, Lowe A, Jain U, Katzman MA, Shen J, Perelman B, Shapiro CM (2004) Acupuncture increases nocturnal melatonin secretion and reduces insomnia and anxiety: A preliminary report. *J Neuropsychiatry Clin Neurosci*. 16:19–28.

Sugiyama Y, Xue YX, Mano T (1995) Transient increase in human muscle sympathetic nerve activity during manual acupuncture. *Jpn J Physiol*. 45:337–345.

Tarrier N, Pilgrim H, Sommerfield C, Faragher B, Reynolds M, Graham E, Barrowclough C (1999) A randomized trial of cognitive therapy and imaginal exposure in the treatment of chronic posttraumatic stress disorder. *J Consult Clin Psychol*. 67:13–18.

Temple R (1989) Government viewpoint of clinical trials of cardiovascular drugs. *Med Clin North Am*. 73:495–509.

Tsui P, Leung MCP (2002) Comparison of the effectiveness between manual acupuncture and electro-acupuncture on patients with tennis elbow. *Acupunct Electrother Res*. 27:107–117.

Ulett GA, Han S, Han JS (1998) Electroacupuncture: Mechanisms and clinical application. *Biol Psychiatry*. 44:129–138.

Van Etten ML, Taylor S (1998) Comparative efficacy of treatments for post-traumatic stress disorder: A meta-analysis. *Clin Psychol Psychother*. 5:126–144.

Wang JQ, Mao L, Han JS (1992) Comparison of the antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat. *Int J Neurosci*. 65:117–129.

Winokur A, Winokur DF, Rickels K, Cox D (1984) Symptoms of emotional distress in a family planning service: Stability over a four-week period. *Br J Psychiatry*. 144:395–399.

Wolpe J (1954) Reciprocal inhibition as the main basis of psychotherapeutic effects. *Arch Neurol Psychiatry*. 72:205–226.

Wolpe J (1958) *Psychotherapy by Reciprocal Inhibition*. Stanford: Stanford University Press.

Yang X, Liu X, Luo H, Jia Y (1994) Clinical observation on needling extrachannel points in treating mental depression. *J Tradit Chin Med*. 14:14–18.