Research Report

THE EFFICACY OF ACUPUNCTURE IN THE TREATMENT OF MAJOR DEPRESSION IN WOMEN

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Abstract—*The effectiveness of acupuncture as a treatment for major depression was examined in 38 women, randomly assigned to one of three treatment groups. Specific treatment involved acupuncture treatments for symptoms of depression; nonspecific treatment involved acupuncture for symptoms that were not clearly part of depression; a wait-list condition involved waiting without treatment for 8 weeks. The nonspecific and wait-list conditions were followed by specific treatment. Five women terminated treatment prematurely, 4 prior to the completion of the first 8 weeks. Following treatments specifically designed to address depression, 64% of the women (n = 33) experienced full remission. A comparison of the acute effect of the three 8-week treatment conditions (n = 34) showed that patients receiving specific acupuncture treatments improved significantly more than those receiving the placebo-like nonspecific acupuncture treatments, and marginally more than those in the wait-list condition. Results from this small sample suggest that acupuncture can provide significant symptom relief in depression, at rates comparable to those of psychotherapy or pharmacotherapy. Acupuncture may hold sufficient promise to warrant a larger scale clinical trial.*

Depression is an unfortunately common condition for which people often seek alternative treatment (Eisenberg et al., 1993). Lifetime-prevalence estimates of major depression (American Psychiatric Association, 1994) have ranged from 3% to 6% (Horwath & Weissman, 1995; Myers et al., 1984; Robins et al., 1984), with recent estimates (Kessler et al., 1994) notably higher, in the range of 17%. The costs of major depressive disorder exceed those of other chronic diseases such as diabetes and hypertension in terms of personal distress, lost productivity, interpersonal problems, and suicide (Gotlib & Beach, 1995; Hirshfield & Schatzberg, 1994).

Conventional treatments for depression, such as psychotherapy and pharmacotherapy, provide significant relief for approximately 50% to 70% of patients who complete treatment. Unfortunately, of those enrolling in treatment, about one third terminate treatment prematurely (Elkin et al., 1989), citing factors such as dissatisfaction with their current treatment or intolerable side effects. If both noncompleters and nonresponders are taken into account, more than half of all depressed persons who enter treatment fail to recover. Even among those who recover from an episode of major depression, more than one third show clinical relapse within 18 months (Shea et al., 1992).

These statistics suggest that alternative treatments may be welcomed by individuals with depression. Such alternatives might serve as adjuncts to or substitutes for existing treatments, or as maintenance or preventive treatments following remission. A recent survey (Eisenberg et al., 1993) revealed that depression was among the 10 most frequently reported medical conditions for which respondents sought treatment, and among those with self-reported depression, seeking alternative treatments (with or without traditional treatment) was more common than seeking the services of a traditional provider alone.

The present study therefore sought to assess the efficacy of an alternative treatment—acupuncture—for major depression. Although abstracts of several reports from China and the former Soviet Union suggest that acupuncture may assist in the treatment of emotional disorders, including those for which depression is a prominent symptom (Chengying, 1992; Cherkezova & Toteva, 1991, 1993; Dudaeva, 1990; Frydrychowski, Landowski, Watrobski, & Ostrowska, 1984; Han, 1986; Polyakov, 1988; Suobin, 1991), there exist no controlled studies of acupuncture's effectiveness for depression in the refereed literature in English.

Acupuncture treatments derive from the principles of Chinese medicine. Strictly speaking, depression does not exist as a disease category in Chinese medicine, because Chinese medicine does not focus on the diagnosis and treatment of disease, but rather on the detection of energetic imbalances. Chinese medicine views health as a balance between the yin and the yang forces, which depends on the proper circulation of the vital energy Qi (pronounced "chee") along energetic pathways or meridians. Within the Western framework, many different symptom patterns are subsumed under the diagnosis major depression (e.g., a depression with overeating, hypersomnia, and psychomotor retardation vs. a depression with loss of appetite, insomnia, and psychomotor agitation); by contrast, these different symptom constellations would signify different patterns of disharmony from the perspective of Chinese medicine, and would require different treatments. The rationale of Chinese medicine has been well described (Kaptchuk, 1983), and we have elsewhere discussed in greater detail its application to assessing and treating depression (Allen & Schnyer, 1998). In brief, acupuncture can be seen as providing a framework for understanding heterogeneous symptom patterns, and for providing treatments individually tailored to address these distinct patterns.

In the present study, patients with major depression received acupuncture treatments that were individually tailored, according to the principles of Chinese medicine, to specifically address each individual's pattern of symptoms. Some patients, prior to receiving these specific treatments, received superficially similar placebo-like treatments designed to treat symptoms other than depression (nonspecific treatments) or entered a wait list. This design allowed us to test whether acupuncture designed to specifically treat symptoms of depression would demonstrate efficacy compared with a wait-list control and nonspecific acupuncture treatments.

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METHOD

Patients

Thirty-eight women between the ages of 18 and 45 were recruited through newspaper advertisements. Advertisements mentioned treatment for depression, but not acupuncture. Patients were included if they met the diagnostic criteria for current major depression as outlined in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; American Psychiatric Association, 1994). They were assessed using the Structured Clinical Interview for DSM-III-R (SCID; Spitzer, Williams, Gibbon, & First, 1990), which was administered by interviewers with a master's in psychology under the supervision of the first author. Patients were excluded if any of the following criteria were present: (a) dysthymia or chronic (duration greater than 2 years) major depression, (b) any current Axis I diagnosis besides major depressive disorder, (c) history of psychosis or mania, (d) substance abuse or dependence within the past 4 months, (e) any current treatment, (f) endocrine abnormalities, (g) history of central nervous system lesions or any medical disorder or treatment that could cause depression, (h) active suicidal potential necessitating immediate treatment, or (i) pregnancy. Five women (13%) dropped out of the study prior to completing it,[1] resulting in a final sample of 33 women who received treatment specifically for depression.

To assess the women's depression, we administered a 31-item, modified version of the Hamilton Rating Scale for Depression (HRSD) modeled after the revision of the HRSD by Gelenberg et al. (1990). Because only 19 of the items in this version address DSM-IV symptoms of depression, we report in this article scores for this subset of items, which we refer to as the DepHRSD.[2] The 33 women in the final sample had mild to moderate depression, with a mean DepHRSD score of 25.1 ($SD = 6.8$, range: 13–41). The mean duration of their current episodes was 9.2 months ($SD = 6.9$), and they had on average 2.5 ($SD = 2.9$) prior episodes. Additionally, 82% of the patients reported having previously received psychotherapy, 53% reported previous trials of antidepressants, and 11% reported no previous treatment. Fifty-nine percent of these patients reported that one or more first-degree relatives also had depression of comparable severity. All participants provided informed consent to participate, and had their rights protected by procedures approved by the University of Arizona's human subjects committee.

General Design and Data Analysis

Factors not specific to acupuncture or the points selected can have therapeutic impact. Such factors include, among others, the patient–acupuncturist relationship and actively engaging in activity believed to improve depression. Our design therefore provided for the development of two types of acupuncture treatments for each patient: a treatment individually tailored to treat the patient's specific symptoms of depression (specific treatment) and a placebo-like treatment designed to treat a pattern of disharmony that was not related to the individual's depression, but was characteristic of the individual (nonspecific treatment; e.g., targeting back pain). The nonspecific treatment was not, strictly speaking, a placebo because it was an active treatment and may therefore have had more impact than a truly inert placebo treatment. We reasoned that if specific treatments outperformed these active nonspecific treatments, it is likely that they would also outperform a truly inert placebo treatment. Active nonspecific treatments were employed, however, to keep the acupuncturists' expectancies of efficacy comparable between the two treatments. Moreover, the specific and nonspecific treatments were similar from the perspective of the patients—involving points in the same general body regions—and patients were unaware of which treatment they were receiving. If specific treatments demonstrated greater efficacy than nonspecific treatments, it would be reasonable to conclude that the effect of acupuncture per se was responsible.

The specific and nonspecific treatment plans were developed according to our treatment manual (Schnyer & Allen, 1998) by an assessing acupuncturist (R.N.S.), and were administered by four other trained and board-certified acupuncturists. Because the nonspecific treatments involved valid acupuncture points, the treating acupuncturists perceived that they were providing a valid treatment, a belief that they would not have held if sham points had been used as a control. The treating acupuncturists were blind to the experimental hypotheses and the method by which the specific and nonspecific treatments were devised, and were not informed of which treatment plan they received. Nonetheless, it may not be appropriate to consider this study fully double-blind because it remains possible that the acupuncturists developed some awareness of the differences between the treatments. There is evidence, however, that the acupuncturists were effectively blinded. They rated their beliefs about the efficacy of the treatment[3] following the first treatment session, and these ratings did not differ between specific and nonspecific treatments, $F(1, 22) < 1$, n.s.

Patients were randomly assigned to one of three conditions (specific treatment: $n = 12$, nonspecific treatment: $n = 11$,[4] or wait list: $n = 11$) and to one of the acupuncturists. All women received the specific treatment. Patients in the specific-treatment group received 8 weeks of specific treatment immediately. Patients in the nonspecific-treatment group received 8 weeks of nonspecific treatment first, and then 8 weeks of specific treatment. Patients in the wait-list group waited 8 weeks before receiving 8 weeks of specific treatment. Each 8-week treatment regimen (both specific and nonspecific) comprised 12 treatment sessions: 2 sessions a week for the first 4 weeks followed by 1 per week thereafter.

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1. Two dropped out for reasons unrelated to treatment (pregnancy, moving out of state), 2 left because of discomfort with the treatment, and 1 left because she was not losing weight and believed that she would lose weight with a pharmacological treatment.

2. The 19 items included in the DepHRSD are depressed mood, suicidal thinking, suicidal behavior, difficulty falling asleep, middle-of-the-night awakening, early-morning awakening, hypersomnia, loss of interest, loss of pleasure, psychomotor retardation, psychomotor agitation, loss of energy, appetite change, weight change during the past month, loss of sexual interest, decreased concentration, helplessness, hopelessness, and worthlessness-failure. The non-included items on the HRSD reflect symptoms such as anxiety (psychic anxiety, somatic anxiety, obsessive-compulsive symptoms) and other nondepressive symptoms (e.g., paranoia, depersonalization).

3. The acupuncturists used a 9-point Likert scale to rate the following two items: "To what extent do you feel you have helped this client?" and "Predict the extent to which the client will benefit from the specific treatment we are offering."

4. Among the 5 patients who left the study prematurely, 2 dropped out from specific treatment, 2 from nonspecific treatment, and 1 from the wait list. The patient who dropped out because she wanted to lose weight had completed nonspecific treatment but had not begun specific treatment, and is therefore included in analyses involving the nonspecific treatment.

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Assessments

Interviews

All patients were interviewed by trained raters blind to treatment condition using the previously described 31-item version of the HRSD. Patients were interviewed before treatment (baseline), after 4 weeks, after 8 weeks, and if in the wait-list and nonspecific groups, after 12 weeks and after 16 weeks. An intraclass correlation of .96 was obtained for a sample of 22 interviews comparing the original interviewers' HRSD scores with consensus (original interviewer excluded) HRSD scores. The questions from the depression section of the SCID were also administered at the end of each 8-week treatment regimen.

Self-report measures

The Inventory of Depressive Symptomatology (IDS; a self-report version of the HRSD; Rush, Giles, Schlesser, & Fulton, 1986), the Beck Depression Inventory (BDI; Beck, Rush, Shaw, & Emery, 1979), and the Beck Hopelessness Scale (BHS; Beck, Weissman, Lester, & Trexler, 1974) were filled out weekly by patients during treatment, but not during the wait-list period. Although the interview data were available for all 33 patients, self-report data were available for 29 women.

RESULTS

First, to test for the efficacy of the specific treatment compared with the nonspecific treatment and the wait list, we examined the reduction in depressive symptoms after Week 8 for all three groups. Second, to estimate the clinical significance of treatment, we calculated the percentage of patients experiencing remission. In all cases, parametric tests are reported, unless the test could not be run because of violations of the normality assumption, in which case the comparable nonparametric test is reported (χ^2 with Friedman repeated measures analysis of variance [ANOVA] on ranks for repeated measures analyses, H with Kruskal-Wallis ANOVA on ranks for nonrepeated measures analyses). All post hoc tests used the Student Newman-Kuels procedure.

Comparative Efficacy of Specific Acupuncture Treatments

To determine whether specific treatment was comparatively more effective than nonspecific treatment or the wait list, we examined change scores from baseline to Week 8. Change scores were selected because, despite random assignment to group, there were significant differences between the groups at baseline on the DepHRSD, $F(2, 31) = 4.6$, $p < .05$: The nonspecific group (mean score = 20.5, $SD = 4.5$) was significantly less depressed ($p < .05$) than both the wait-list group (mean score = 27.7, $SD = 6.8$) and the specific group (mean score = 26.9, $SD = 6.7$), which did not differ from one another.

Figure 1 shows the mean change in DepHRSD scores for the three groups over the course of the study. A one-way ANOVA revealed a significant difference in symptom reduction between the groups on the DepHRSD, $H(2) = 7.2$, $p < .05$. The symptom reduction in the specific group ($M = -11.7$, $SD = 7.3$) exceeded that of the nonspecific group ($M = -2.9$, $SD = 7.9$). In addition, there was a nonsignificant trend ($p < .12$) for symptom reduction in the specific group to exceed
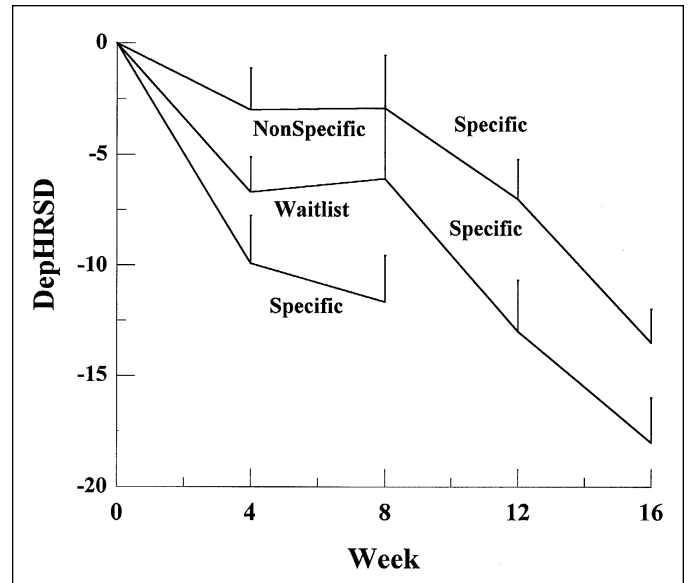
Fig. 1. Mean ($\pm SE$) change on the depression items from the Hamilton Rating Scale for Depression (DepHRSD) for patients in the specific-treatment ($n = 12$), nonspecific-treatment ($n = 11$), and wait-list ($n = 11$) groups by week. Note that after 8 weeks, patients in the nonspecific-treatment and wait-list groups began receiving specific treatment.

that of the wait-list group ($M = -6.1$, $SD = 10.9$). Similar results were obtained over the 8-week interval with the self-report measures for those patients undergoing treatment. On the BDI, patients in the specific group demonstrated larger changes ($M = -10.7$, $SD = 7.8$) than those in the nonspecific group ($M = -3.4$, $SD = 7.4$), $F(1, 20) = 5.2$, $p < .05$. On the IDS, patients in the specific group also demonstrated larger changes ($M = -18.5$, $SD = 11.8$) than those in the nonspecific group ($M = -8.5$, $SD = 9.0$), $F(1, 20) = 5.0$, $p < .05$. No differences emerged on the BHS, $F(1, 20) = 1.3$, n.s. Because self-report measures were completed only in the context of treatment, no comparisons with the wait-list condition were possible using self-report measures.

To determine whether the results would be the same for the original intent-to-treat sample, we conducted two analyses. The simple intent-to-treat analysis took the last available DepHRSD score of each participant who dropped out and carried that score forward to count as the subsequent observation. DepHRSD scores again differed significantly between participants in the three treatment groups, $H(2) = 6.4$, $p < .05$. The second strategy used a random regression model (Gibbons et al., 1993, implemented with BMDP 5V), which imputes missing values based on maximum-likelihood estimates of missing parameters, thereby allowing for the analysis of all intent-to-treat subjects. The model examined DepHRSD scores at intake, 4 weeks, and 8 weeks, and revealed a significant Group × Time interaction ($\chi^2[4, N = 38] = 9.70$, $p < .05$), which indicated that the rate of change differed significantly between the specific- and nonspecific-treatment groups ($\chi^2[2, N = 26] = 9.95$, $p < .01$), but not between the nonspecific-treatment and wait-list groups ($\chi^2[2, N = 24] = 0.76$, n.s.). The specific-treatment and wait-list groups showed a trend for rates of change to differ, $\chi^2(2, N = 26) = 4.28$, $p < .12$.

Clinical Significance

We used two measures to ascertain whether treatment resulted in clinically significant remission: DSM-IV diagnoses and at least a 50% reduction in scores on the DepHRSD. Full remission in terms of DSM-IV diagnoses was defined as absence of both core symptoms of depression (depressed mood and anhedonia).

At the conclusion of the acute (8-week) phase of treatment, by DepHRSD criteria, 50% of the participants in the specific-treatment group had remitted, whereas only 27% in the nonspecific-treatment group and 27% in the wait-list group had remitted. By DSM-IV criteria, 42% of those in the specific-treatment group, 9% of those in the nonspecific-treatment group, and 20% of those in the wait-list group had experienced full remission.

After completion of specific treatment (pooled across all patients), by DepHRSD criteria, 70% of women had remitted. Using the DSM-IV remission criteria, 64% of women experienced full remission.

DISCUSSION

These findings from a small sample of women with major depression suggest that acupuncture may hold sufficient efficacy to warrant a larger clinical trial. Moreover, it appears that acupuncture induces remission at rates roughly comparable to those of conventional treatments[5] (Elkin et al., 1989). Additionally, the dropout rate of 13% in this sample compares favorably with the rates of more than 30% reported in other studies (Elkin et al., 1989), although such a finding could be due to many factors that may or may not be related to the modality of treatment. It is important to note that all women in this study were outpatients, free of psychosis or acute suicidal ideation. However, 29% of them met criteria for suicidal ideation (but without acute risk), based on the SCID. The efficacy of acupuncture for more severe depressions is unknown.

The present data also suggest that acupuncture has a specific effect above and beyond the nonspecific therapeutic factors related to regular visits to an acupuncturist. Patients receiving specific treatment improved more over 8 weeks than patients receiving nonspecific treatment. Although expectancy effects cannot be completely ruled out as a factor in the comparative efficacy of the treatments, the design minimized the possible role of these effects. Patients were blind to which treatment they received. Moreover, the treating acupuncturists implemented treatment plans provided by the assessing acupuncturist, and both the specific and the nonspecific treatments involved active and valid acupuncture points. Furthermore, the acupuncturists' beliefs about the efficacy of the treatment—which were assessed following the first treatment session—did not differ between specific and nonspecific treatments, reducing the likelihood that the acupuncturists'

expectancies were responsible for the observed superiority of the specific treatment. Although it remains possible that the treating acupuncturists' expectations changed across the 8 weeks of delivering treatment, it would be impossible to determine whether differential beliefs about the effectiveness of specific and nonspecific treatment—if such beliefs had been assessed later in the progression of treatment—would indicate unblinding or simply be the result of differential improvement in the specific- and nonspecific-treatment groups.

Because specific treatment did not produce significantly greater improvement than the wait list, it remains possible that the improvement during specific treatment was due to spontaneous remission. Several findings suggest, however, that the specific treatment may have provided improvement above and beyond that expected by spontaneous remission alone. First, spontaneous remission was equally likely to affect patients in all groups, and specific treatment provided greater improvement than nonspecific treatment. Moreover, an examination of the effect sizes[6] indicates that the relative advantage of the specific treatment over the wait list ($d = 0.61$) is similar to what has been observed when other treatment modalities have been compared with a wait-list control in depression (Robinson, Berman, & Neimeyer, 1990). With greater statistical power, specific treatment would likely prove significantly more effective than a wait-list control, as the power to detect a significant difference between these two groups with the present sample size is only .31. Finally, among participants in the wait-list group, comparing the change observed during the specific-treatment phase and the wait period preceding it yields an effect size ($d = 0.52$) of similar magnitude. In other words, even after 8 weeks of a wait list, specific treatment provided change that was notably larger than that seen in these same patients during the wait period. Similarly, specific treatment produced larger change than the nonspecific treatment preceding it ($d = 0.79$) for patients in the nonspecific-treatment group (see Fig. 1).

These findings are, of course, preliminary. Larger scale studies are required to provide corroboration. If additional research corroborates that acupuncture is an effective treatment for depression, further research should address several issues. First, acupuncture's effectiveness remains to be determined for severe or chronic depressions (e.g., chronic major depression, dysthymia), as well as for persons with comorbid disorders (e.g., anxiety disorders, substance dependence). Second, the long-term prognosis of patients who respond to acupuncture treatment is unknown. Therefore, future research can address whether the treatment gains are maintained or whether less-frequent continuation or maintenance treatments are required after the initial set of treatments. Evidence from studies of other treatments for depression suggests the importance of maintenance treatments (Hirshfield & Schatzberg, 1994). Third, a direct comparison of the efficacy of acupuncture and psychotherapy or pharmacotherapy—within the same study—needs to be performed. Fourth, investigation of the mechanisms by which acupuncture achieves its effects is required. Finally, and perhaps most important, future research is required to determine whether acupuncture can assist individuals who fail to respond to traditional treatments, and whether traditional treatments will assist those who fail to respond to acupuncture.

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5. Remission criteria vary somewhat from study to study. Very few studies have used interview-based DSM diagnoses as a measure for remission because the interviews are expensive and labor-intensive. Most studies use a joint criterion of reduction of 50% in HRSD score and a final score less than or equal to 6. The present data cannot be compared with data from studies using this criterion because we used a version of the HRSD that is different from the version most studies use. BDI scores, however, can provide a clear comparison between the results in this study and those reported in the literature. After the 33 patients had completed specific treatment, their mean BDI score was 12.1, which compares favorably with the mean score of 11.8 from 22 studies of psychotherapy (Robinson, Berman, & Neimeyer, 1990).

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6. Effect sizes were calculated using Cohen's (1977) d, which expresses the differences in treatment means as a proportion of the pooled standard deviation: $(\bar{x}_1 - \bar{x}_2)/s$, where $\bar{x}_1$ is the first treatment mean, $\bar{x}_2$ is the second treatment mean, and s is the pooled standard deviation.

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