Electrosleep Therapy

A Double-Blind Trial

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Twenty-eight patients participated in a controlled double-blind study to determine the effectiveness of electrosleep as a treatment modality. To our knowledge this is the first study in the English literature in which the peripheral rhythmic electrical stimulation has been eliminated, thereby allowing the results of the current effect on the brain to be independently evaluated.

Both global ratings by patients and physicians on the fifth day of treatment and on two-week follow-up indicate that current effect is not associated with significant improvement, although patient global ratings on day 5 indicate a trend in this direction. Self-rating scales by patients indicate no significant improvement for anxiety, insomnia, or somatic complaints. Depressive self-rating scales do show a significant improvement on day 5 of treatment, but no carry over effect to the two-week follow-up.

Electrosleep therapy, as introduced by Giljarowski, is one of the features of Russian psychiatry that has attracted the greatest interest in the United States.[1] In the past decade, several uncontrolled American studies have concluded that it is effective in the treatment of symptoms of anxiety, depression, insomnia, migraine headaches, and gastric distress in patients from a wide range of personality disorders, neuroses, affective disorders, or schizophrenia.[2,3] More recently two double-blind controlled studies using a crossover design have been reported that suggest that certain patients may do better with electrosleep therapy than with other current treatment modalities.[4,5] In both studies the patients who showed improvement had prominent anxiety, depression, and insomnia.

Based on available data it is not possible to determine if the type of "simulated treatment" used in these studies really constitutes an appropriate control. In these studies the active treatment group received electrical current to the skull and also experienced a "tingling" peripheral sensation at the electrode site throughout each treatment session whereas the control group received neither electrical current nor peripheral stimulation. Such a control is probably adequate if one assumes that the therapeutic modality is a direct cerebral effect of electrical current.

However, there are two conflicting schools of thought regarding the cause of treatment response. Electrophysiologists contend that the therapeutic effect is caused by electricity acting directly on the brain though most of the electrical current does not reach the brain because it travels through skin, muscle, and bone. However, studies done with implanted electrodes in man have shown that a certain amount does travel through to reach the frontal lobes and brain stem.[6,7] Kalinowsky questions the importance of any direct cerebral effect: "What is emphasized as being therapeutically useful is the rhythmic nature of a peripheral stimulation which indirectly produces sleep even when the electrodes are applied to the legs."[8] If suggestion, setting, and peripheral stimulation are in fact the critical therapeutic variables, it is not surprising that patients who experience a tingling sensation through each session should do better than the others who experience no peripheral stimulation. It is also clearly more difficult to eliminate suggestion when the operator and the subject can discriminate easily between treatment and placebo sessions.

In order to evaluate the cerebral effect of electrical current independently from the effect of a rhythmic peripheral stimulus one must design a protocol in which the amount and type of peripheral sensation is the same for both the treatment and placebo group. This report presents the results of such a study in which both treatment and follow-up phases were carried out in a strict double-blind fashion with a group of systematically interviewed, chronically ill psychiatric outpatients.

Method

Patient Selection.—Patients were considered for inclusion in the study if they fulfilled the following criteria: (1) currently attending a Washington University psychiatric outpatient facility for at least one month before treatment; (2) have been continuously psychiatrically ill for two or more years without obtaining a definitive remission despite adequate trial on appropriate chemotherapy and psychotherapy; and (3) no change in chemotherapy, attending psychiatrist, or psychotherapeutic approach for at least one month prior to treatment. Patients were otherwise excluded

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Table 1.—Comparison of Demographic Characteristics of Treatment Groups

	Active Treatment	Sham Treatment
Total No.	14	14
Sex		
No. of men	3	1
No. of women	11	13
Race		
No. of blacks	4	4
No. of whites	10	10
Age		
Range, yr	20-61	20-60
Mean, yr	37	40

Table 2.—Comparison of Primary Psychiatric Diagnoses of Treatment Groups

Psychiatric Diagnosis	Active Treatment, N = 14	Sham Treatment, N = 14
Hysteria	4	7
Primary affective disorder	3	1
Anxiety neurosis	1	2
Obsessional neurosis	1	2
Antisocial personality	1	0
Chronic renal failure with secondary affective disorder	1	0
Undiagnosed psychiatric illness	3	2

Table 3.—Comparison of the Number of Symptomatic Days Following Active or Sham Treatment: No. of Patients Reporting Greater Than Median Improvement*

	Day 5		Day 19	
Symptom Complex	Active Treatment, N = 14	Sham Treatment, N = 14	Active Treatment, N = 12	Sham Treatment, N = 12
Insomnia	8	6	6	5
Depression	7	6	4	6
Anxiety	4	9	4	5

* Patients reported the number of days they were symptomatic during four-day periods ending on days 1, 5, and 19. They received a quantitative score for each period based on response to questions concerning the number of days they had any or no insomnia (initial, middle, or terminal) "more or less anxiety than usual," and "more or less depression than usual." Scores at the end of treatment (day 5) and two weeks later (day 19) were compared to that for the period preceding treatment (day 1).

only if they were psychotic, had an organic brain syndrome or neurologic disease including seizure disorders and cerebral arteriosclerosis.

All prospective patients were given a typed set of instructions explaining the treatment, stating that there were no harmful side-effects and that prior research indicated the treatments might help them. Patients were given no guarantee of improvement and were not informed of the double-blind study design.

Diagnostic Evaluation.—All patients were given a systematic diagnostic interview by one of us. Past psychiatric records were reviewed. A diagnosis was made according to specific criteria.[9]

Instrumentation.—The Neurotone 101 was used. It is a transistorized, battery-powered frequency source that generates a gated sine wave burst of current with no direct current bias. Burst rate was 100 hertz/second with a burst width of 2 msec. This current was used to treat the alternating current treatment group. For the direct current treatment group the output was rectified and filtered to form positive square wave pulses of the same width and frequency.

Output was passed through a specially prepared sequence of two "black boxes." Each box had two sets of dials, one of which was hidden from the machine operator's view. Another technician set the hidden dial to one of two preassigned positions. The other dial was later set by the operator to one of two positions. Depending on the setting of the hidden dial the same setting by the operator might result in either of two possible outcomes: box 1 determined current or no current while box 2 determined alternating or direct current if current was given. The operator determined the proper current amplitude by using a third dial position that always resulted in current flow and then changed the settings to that of the randomly assigned treatment position.

Patient Assignment and Preparation.—The first 22 patients were randomly assigned to either an alternating current treatment group or a sham treatment group. The remaining patients were randomly assigned to either an alternating current treatment group, a direct current treatment group, or to sham treatment.

Treatment set up and preparation was the same for all patients. Operating instructions and electrode placements (suggested by Neuro Systems Inc.), were followed. When and if rectified the electrodes on the supraorbital ridge were cathodes and those on the mastoid processes were anodes. Particular care was taken in preparing the skin and applying the electrodes in order to reduce the skin impedance as much as possible and thereby minimize the peripheral sensation. Skin was cleaned with alcohol swabs and rubbed until there was local erythema. A thin layer of DB electrode paste was applied as vigorously as possible without noticeably abrading the skin. Electrode pads were immersed in normal saline then held in place with specially made elastic headbands secured as tightly as possible without causing discomfort.

Patients sat in a reclining chair situated in a semidarkened quiet room. After electrodes were placed the amplitude of current was increased over a 30-second period to the point of the patient's tolerance of the tingling sensation. Then the amplitude was gradually diminished over a 30-second period to an amplitude just below the threshold at which the patient reported no peripheral sensation other than the presence of the electrode pad and were unable to detect any change if the current output was abruptly turned to 0. In practice this same current would result in a definite tingling sensation if the headband securing the electrodes was not as tight and no electrode paste was used. Excluding the patients who received only sham treatments, the current amplitude ranged from 0.30 ma to 1.1 ma with a mean of 0.64 and a standard deviation of ± 0.18. After the final setting was made the amplitude was covered and the dial on box 1 set to a randomly assigned position that determined active treatment or placebo. Treatments lasted 30 minutes and were administered for five consecutive days.

Assessment.—Assessment of clinical change was made using the National Institute of Mental Health (NIMH) self-rating symptom scale (SRSS) and by global rating scales for sleep, anxiety, depression, and overall status. These evaluations were made on the first day of treatment, the last day of treatment, and two weeks following the last treatment day. Four patients could not be located for the two-week follow-up. In addition to the patients' global ratings, the physician who originally interviewed the patient reported his own global ratings on a blind basis for day 5 of treatment, and for the two-week follow-up. Three subsets of questions were selected from the SRSS in order to evaluate individually symptom clusters of anxiety, depression, and somatic complaints. Those patients who clearly failed to respond to treatment and who remained unchanged at the two-week follow-up were dropped

Table 4.—Comparison of the Extent to Which Patients Were Bothered or Disturbed by Their Symptoms Following Active or Sham Treatment: No. of Patients Reporting Greater Than Median Improvement*

Symptom Complex	Day 5		Day 19	
	Active Treatment, N = 14	Sham Treatment, N = 14	Active Treatment, N = 12	Sham Treatment, N = 12
Depression	11†	3	6	5
Anxiety	4	7	6	6
Hypochondriasis	4	6	6	6

* On self-rating symptom scale, symptoms are listed and patients report "how much the symptoms bothered or disturbed you during the past four days, not at all, a little, quite a bit, or extremely." Quantitative scores were determined on days 1, 5, and 19 and the latter two scores each compared to the former.

† Patients who received active treatment were significantly less distressed by depressive symptoms on day 5 than were patients who received sham treatment ($P < .05$).

from further follow-up. Those who responded or whose response was questionable were followed at two-week intervals until they had relapsed with no sign of improvement.

All statistical analyses were done using Fisher's exact test for 2×2 contingency tables.

Results

Patient Characteristics.—A total of 28 patients were equally divided into active treatment and sham-treatment groups. Eleven patients received active treatment with alternating current and three patients received active treatment with direct current. The demographic characteristics of both active and sham groups are shown in Table 1. The two groups were comparable in age and in race; the active-treatment group contained three of the four men in the study.

All the subjects were chronically ill psychiatric outpatients with prominent anxiety and depression. Their primary psychiatric diagnoses were heterogeneous, as shown in Table 2. Hysteria was the most frequent diagnosis in each treatment group but the active treatment group contained relatively fewer hysterics and more primary depressives.

Response to Treatment.—The two groups were compared according to the number of days they were symptomatic following treatment (Table 3). Both groups improved relative to the pretreatment period, but they did not differ substantially either on the last day of treatment or two weeks later.

The groups were also compared according to the extent to which they were bothered or distressed by their symptoms following treatment (Table 4). At day 5 of treatment, the groups did not differ greatly in their tolerance of somatic or anxiety symptoms. The patients receiving active treatment were significantly less depressed than the patients receiving sham treatment (79% vs 21%, $P < .05$). The depressive symptom complex was further analyzed according to individual symptoms. The active treatment group had an excess of improved patients according to 12 of the 18 depressive symptoms, but no individual symptom showed a difference significant at the 5%

Table 5.—No. of Patients Who Were Better or Completely Well on Overall Global Ratings

	Day 5		Day 19	
	Active Treatment, N = 14	Sham Treatment, N = 14	Active Treatment, N = 12	Sham Treatment, N = 12
Patient's global ratings	11*	7	4	5
Physician's global ratings	6	3	2	2

* $P < .10$.

confidence level. Comparing the two groups on day 5, there was a trend ($P < .10$) for more improvement following active treatment in three individual symptoms: feeling lonely (64% vs 21%), having feelings easily hurt (64% vs 21%), and difficulty falling asleep or staying asleep (71% vs 29%). Two weeks after treatment the two groups had no differences in their reports of individual symptoms of symptom complexes.

The two groups were also compared according to their global self-ratings and global physician ratings (Table 5). According to both the patients and the physician, patients receiving active treatment were more often improved overall on the last day of treatment than were the others, but the differences were not significant. Self-ratings revealed the greater differences (79% vs 50% $.10 > P > .05$). But once again two weeks later there was no overall difference between the groups.

Longer follow-up was more discouraging. Only two patients were improved beyond two weeks posttreatment; one relapsed after one month and the other after two months. A third patient showed marked improvement for one week following treatment then relapsed for three weeks until she again responded to biweekly maintenance therapy for an additional two months. This patient was the only subject who volunteered for retreatment. All three patients with improvement sustained beyond two weeks had received active treatment.

Comment

The response of our patients to electrosleep therapy was not impressive. Patients receiving active treatment did report significantly less distress from their depressive symptoms during the week of treatment than did the patients who received sham treatment. However, a comparison of the number of days that they were symptomatic before and after treatment revealed no differences between the two groups. Also, there was no acute relief of anxiety and no persistent improvement in overall status beyond two weeks except in two patients. The data suggest that either electrosleep may transiently increase the patient's tolerance of their depressive symptoms without significantly altering symptom frequency, or that it has a transient mild effect on both symptom frequency and intensity without any appreciable change on the natural course of the illness. The lack of any marked clinical response is perhaps reflected by the fact that only one patient volunteered for retreatment. The fact that two of the 14 pa-

tients who received active treatment did show improvement does suggest that an occasional patient may do better with this treatment modality than with others but the number is indeed small and must await confirmation in trials with a larger patient population.

Our results are similar to those of Feighner et al[5] in that the treatment response, when present at all, is transient with relapse within one month seen in nearly all patients. However, the symptoms which Feighner found to respond initially differ from our experience. He concluded that "active electrosleep therapy significantly improved the target symptoms, particularly insomnia and anxiety." Seven of his 14 anxiety neurotics showed significant improvement initially, whereas four of six subjects with primary affective disorder were adversely affected by treatment. In our experience only the depressive symptoms showed any significant change, and no patient with primary affective disorder was adversely affected. In fact, our longest sustained improvement was a two-month remission in a woman with a primary depression of 18-years duration. Since Feighner treated patients primarily with anxiety neurosis and few of our patients were so diagnosed, the differences could, in part, reflect different patient populations. Moreover, caution dictates conservative interpretation of results concerning small numbers of patients with a rapidly fluctuating illness like primary affective disorder. We see no contraindication in our data to treating patients with primary affective disorder with electrosleep therapy.

Our results are not nearly as encouraging as those of Rosenthal.[4] He treated 22 patients with various neurotic and personality disorders and concluded that patients receiving active treatment showed "marked clinical improvement that was significantly greater than that showed by patients receiving placebo treatments." His study employed a crossover design. Among the 11 patients who originally received active treatment, eight showed marked improvement; but none of the patients who originally received inactive treatment showed marked improvement with a subsequent course of active treatment. Rosenthal suggested this difference at crossover might be due to nonresponders having a negative expectation following inactive treatment; however, in Feighner's study treatment sequence was not associated with a differential response to treatment. This later observation suggests that Rosenthal's treatment groups may not have had a comparable prognosis.

As previously mentioned, it is also questionable whether the type of control used in the earlier crossover studies is adequate. We were able to give the same average current used in the earlier studies while eliminating the peripheral tingling sensation from both active treatment and control groups by reducing skin resistance through the use of electrode paste and increased headband pressure. Thus, the peripheral stimulation experienced by the two groups was the same and the effect of electrical current could be evaluated independently. The differences between the earlier crossover studies and our study underscore the need for further study of the question of patient selection and differential response to treatment among patients from different diagnostic groups.

A number of other important questions remain unanswered by available studies. There have been no systematic comparisons of the efficacy of alternating current vs direct current, of the effect of various concurrent tranquilizers, or of variations in the length and number of treatments. Concurrent medication may have interfered with the response to electrosleep in this study, but so few of our patients showed clinically significant improvement that it would not be productive to try to identify individual factors correlated with improvement within this population. In addition equipment to rectify the alternating current output of the Neurotone 101 was obtained too late for us to treat a sufficient number of cases with each type of current to allow meaningful comparisons. While our results are rather discouraging, they should not be interpreted as a demonstration that electrosleep therapy given to other patient populations with different technique measures will also be ineffective. Rosenthal obtained marked benefit with the same number of treatments we administered (five sessions of 30-minute duration apiece) in patients whose symptoms of anxiety and depression had a mean duration of six months, but other studies of chronically ill patients have demonstrated little or only transient improvement despite ten or more sessions[4,5,10] It is possible that only patients with acute illnesses respond to electrosleep or perhaps that chronic patients require a cumulative effect from many treatments before they respond. Further systematic work on electrosleep is needed to elucidate these serious technical problems. Our results emphasize the need for such work to be carried out with strict controls under true double-blind conditions.

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