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THE PLACEBO EFFECT OF TRANSCUTANEOUS ELECTRICAL STIMULATION

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SUMMARY

The placebo effect of transcutaneous electrical stimulation was studied in 93 patients in a double-blind cross-over trial using a genuine stimulator and a placebo machine. Placebo analgesic effects occurred in 32% of trials, as compared with 48% for actual stimulation. The placebo effect of the transcutaneous electrical stimulator is similar to the placebo effect that is noted in other double-blind studies in which medications are used.

INTRODUCTION

The evaluation of therapy in controlling pain is not easy. The therapeutic effect can be measured by relying on the patients' reports in relation to an arbitrary measurement scale of subjective responses [1,2]. One could observe changes in emotion, behavior, autonomic function, or pain threshold. These measurements are subjected to numerous variables, making evaluation difficult [2,9]. A different approach is to use a double-blind design in which the control group receives an inert therapy. In this way, the actual therapy can be assessed to determine whether its effects exceed those due to the expectation and hope in both the patient and the person administering the therapy [2].

Review of a number of clinical trials [2,10] has indicated that about 36% of patients who suffer from pain are effectively relieved by a placebo. The placebo effect is directly proportional to the apparent effectiveness of the active agent both in dose response and time effect [2]. When introducing a new analgesic agent the placebo effect must be evaluated. Previous studies on transcutaneous electrical stimulation have not included double-blind trials [4,6,8,11,12].

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METHOD AND MATERIALS

The effectiveness of transcutaneous neurostimulation (TNS) was studied in outpatients who had chronic pain. Patients included in the study had chronic pain lasting longer than 1 month, had had a complete medical work-up, and had consented to enter the study. Each patient was similarly instructed according to a previously prepared outline. These instructions included informing the patient that the study was a double-blind trial and instructing each to differentiate between the sensation experienced during stimulation and the relief of pain. The therapists applying the device were given the same instructions as those given to the patient and were instructed in the application of the stimulator *. The placebo machines were identical in appearance but had no electrical output to the electrodes.

Each patient had 3 treatment sessions with the stimulator and 3 treatment sessions with the placebo for a total of 6 treatments, each at a different time. Every patient received either all of the stimulator treatments first or all of the placebo treatments first. The sites treated with each device were (1) over the center of pain, (2) over the nerve trunk related to the center of pain, and (3) over an unrelated distant nerve trunk. The randomization scheme and the treatment schedule were prepared by the department of statistics. The patient was assigned to this treatment schedule (which had a cross-over design) by the supervisor in physical therapy. The therapist then applied the indicated machine to the indicated site, as prescribed. The physician conducting the study then recorded the results of the treatments as complete relief, partial relief, no relief, or aggravation, according to the patient's response. The duration of these effects was also recorded.

Six machines were used: three were actual stimulators and three were identical-looking machines that gave no stimulations into the electrodes. Only the supervisors, who regularly checked on the conditions of the stimulators, knew which were the stimulators and which were the placebo machines. The supervisors did not apply the devices, and they did not record the results. The applications were done by trained physical therapists who did not give any information about the device or the expectations. The therapists were asked to direct all questions to the physicians, who would see the patient after the sixth treatment. A physician recorded the patient's response. Before the patient entered the study he was told that he might experience tingling numbness or nothing at all. The patient was asked to disregard this and to concentrate only on pain — either to report the relief of pain or the aggravation of pain. No ruse was used. To avoid any bias, the main emphasis was placed on following the protocol and maintaining standard procedures.

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*One type of stimulator was used: the Stimtech EPC Personal Stimulator, which was supplied by the Stimulation Technology Co., Minneapolis, Minn. (this company also supplied the placebo machines).

At the end of the 6 treatments, the supervisor summarized the results and made them available to a second physician (other than the one who recorded the responses), who discussed the continuing use of the stimulator with the patient. The patient was given free choice to continue to use the stimulator, and if he selected to do so, he was instructed in its use. The patient could either rent or buy the stimulator. He had a free choice to use the stimulator over any of the sites that had been treated during the trial. The patient was thoroughly instructed in how to apply the stimulator. A 3-month and a 6-month follow-up were done to determine the continuing use and continuing efficacy of the stimulator.

RESULTS

A total of 107 patients entered the study and 93 (53 women and 40 men) completed the trial. The age distribution for the women and men had the same mean (48.7 years) and the same standard deviation (11.8 years).

More patients claimed to have a single center of pain (63 patients) than multiple centers (30 patients), and constant pain was more often reported (82 patients) than was intermittent pain (11 patients). The major primary diagnostic groups (Table I) were neuropathies (24 patients) and low-back pain syndromes (33 patients). The most common secondary associated diagnoses were surgery (50 patients) and trauma (20 patients).

Of the 93 patients in the study, 83 completed the Minnesota Multiphasic

TABLE I

DIAGNOSES AND DISTRIBUTION ACCORDING TO TYPE OF PAIN

Diagnoses	Number of patients		
	Associated pain		Not associated
	Primary (at site)	Secondary (near site)	
Malignant disease	0	1	1
Trauma	5	20	8
Neuropathy	24	6	2
Arthritis	3	7	5
Amputation	0	1	0
Pelvic floor pain	1	1	1
Other neurologic problems	6	4	2
Surgery	5	50	9
Low-back pain	33	14	4
Neck pain	5	13	1
Psychiatric	0	7	5
Neuroma	3	1	0
Fracture	1	1	1
Other orthopedic problems	7	3	1

Personality Inventory (MMPI). The scores on the first 3 clinical scales of the MMPI were used to classify the 83 patients into 3 personality groups: normal, depressed and hysterical.

The efficacy of the stimulator was evaluated by comparing the effect of the stimulator with that of the placebo for each patient (Tables II, III, and IV). The efficacy of the machines was determined while treatment was being done and subsequent to treatment, and the efficacy was correlated to treatment site, diagnosis, sex and personality characteristics. The stimulator was preferred (better effect) (1) by the overall group while treating over the center of pain ($P < 0.005$), subsequent to treatment over the center of pain ($P < 0.005$), and while treating over an unrelated nerve ($P < 0.01$, Table II); (2) by the group of patients with normal MMPI while treating over the unrelated nerve trunk ($P < 0.005$, Table III); and (3) by the group of patients with neuropathies while treating over the related nerve trunk ($P < 0.01$) and subsequent to treatment over the related nerve trunk ($P < 0.005$, Table IV).

The reported responses to the effects of treatments with the stimulator and the placebo are shown in Fig. 1 (while stimulating = during treatment) and in Fig. 2 (subsequent to treatment). The placebo effect was the highest where the apparent stimulator effect was the highest, when treating over the center of pain. The placebo effect was lower where the apparent stimulator response was lower, when treating over the related nerve trunk. The placebo response was the lowest where the apparent stimulator response was

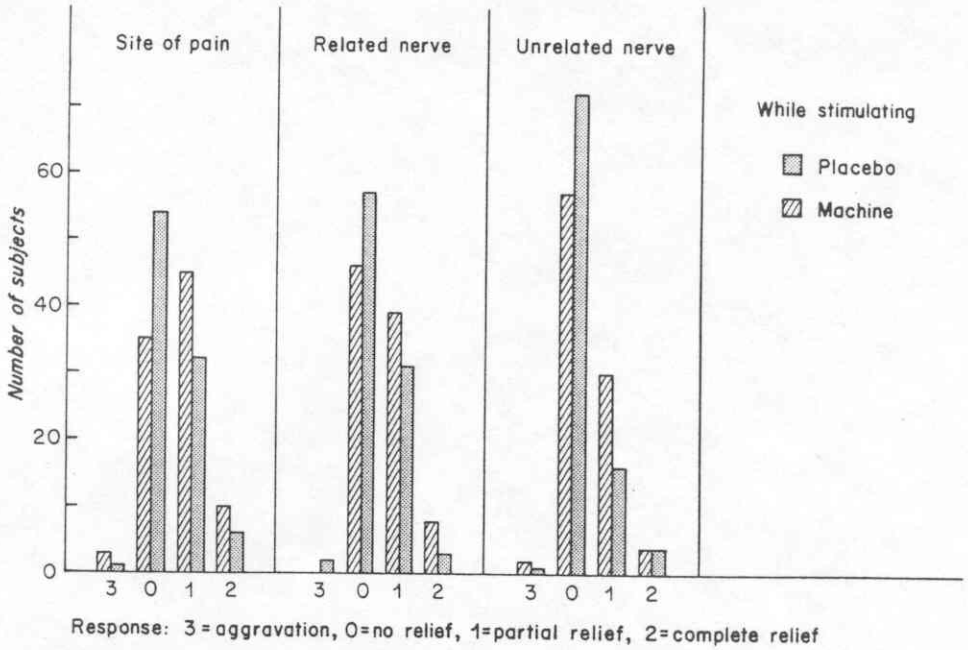

Fig. 1. Responses to stimulator and placebo during treatment. Number of treatments for each site: 93 by the stimulator (machine) and 93 by the placebo device. For claim of significant difference see Table II.

TABLE II

PREFERENCE BY SITE TREATED BOTH DURING AND AFTER TREATMENT (N = 93)

Treatment site	Preference							
	During treatment				After treatment			
	Stimulator	Placebo	None	*P* value	Stimulator	Placebo	None	*P* value
Over center of pain	31	10	52	<0.01	27	8	58	<0.01
Over related nerve	26	11	56	NS	28	12	53	NS
Over unrelated nerve	24	9	60	<0.01	22	10	61	NS

TABLE III

PREFERENCE IN THE PERSONALITY GROUPS AND IN FEMALES AND MALES BY THE SITE TREATED

Group	Site [a]	Preference							
		During treatment				After treatment			
		Stimulator	Placebo	None	*P* value	Stimulator	Placebo	None	*P* value
Normal	CP	11	4	15	NS	10	2	18	NS
MMPI	RN	9	5	16	NS	10	6	14	NS
(N = 30)	UN	11	1	18	<0.01	8	3	19	NS
Hysterical	CP	13	3	14	NS	12	4	14	NS
MMPI	RN	9	3	18	NS	11	4	15	NS
(N = 30)	UN	10	5	15	NS	9	2	19	NS
Depressed	CP	6	2	15	NS	3	2	18	NS
MMPI	RN	8	3	12	NS	4	2	17	NS
(N = 23)	UN	2	2	19	...	3	3	17	...
No MMPI	CP	1	1	8	...	2	0	8	...
(N = 10)	RN	0	0	10	...	3	0	7	...
	UN	1	1	8	...	2	2	6	...
Females	CP	18	6	29	NS	16	5	32	NS
(N = 53)	RN	13	9	31	NS	19	9	25	NS
	UN	14	4	35	NS	14	6	33	NS
Males	CP	13	4	23	NS	11	3	26	NS
(N = 40)	RN	13	2	25	NS	9	3	28	NS
	UN	10	5	25	NS	8	4	28	NS

[a] CP, center of pain; RN, related nerve; UN, unrelated nerve.

TABLE IV

PREFERENCES IN THE TWO MAIN DIAGNOSTIC GROUPS BY SITE TREATED

Group	Site [a]	Preference							
		During treatment				After treatment			
		Stimulator	Placebo	None	*P* value	Stimulator	Placebo	None	*P* value
Neuropathy (N = 24)	CP	9	2	13	NS	9	1	14	NS
	RN	10	1	13	<0.01	11	1	12	<0.01
	UN	10	3	11	NS	7	2	15	NS
Low-back pain (N = 33)	CP	13	4	16	NS	11	2	20	NS
	RN	7	5	21	NS	8	5	20	NS
	UN	6	4	23	NS	6	5	22	NS

[a] CP, center of pain; RN, related nerve; UN, unrelated nerve.

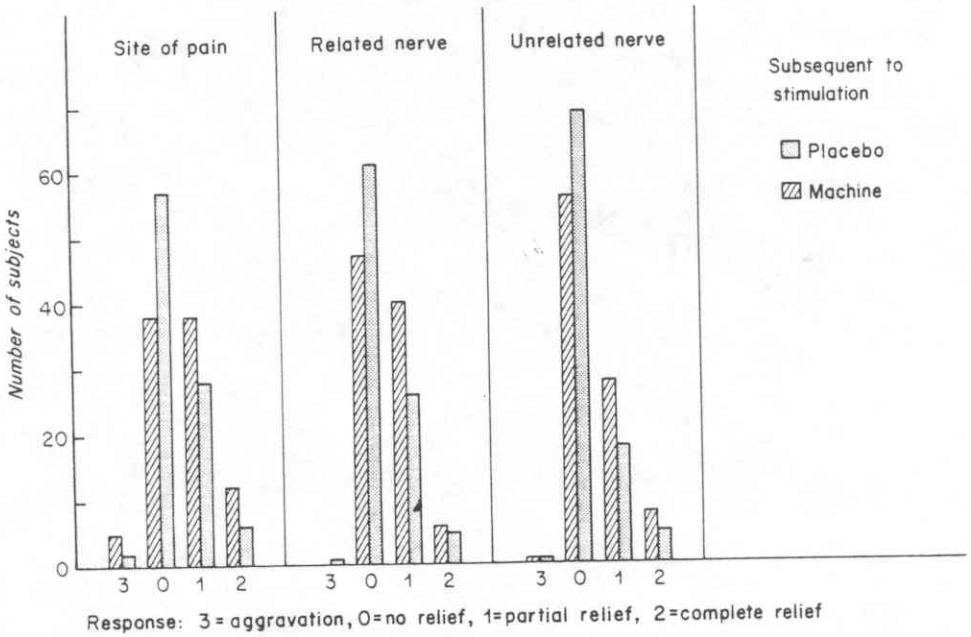

Fig. 2. Responses to stimulator and placebo subsequent to controlled treatment. Number of treatments for each site: 93 by the stimulator (machine) and 93 by the placebo device. For claim of significant difference see Table II.

the lowest, when treating over the unrelated nerve trunk. The highest preference (actual effect) of the stimulator was observed when treating over the related nerve trunk in patients with neuropathies. The mean stimulator effect (successful responses = complete or partial relief) was 48.7% during treatment and 47.3% subsequent to treatment. Corresponding data for the placebo were 33 and 31.5%. The pain was reported to have been aggravated by the stimulator in 11 cases and by the placebo in 8 cases.

Patients reported lasting relief more often after using the stimulator than the placebo, but the difference was not significant. The frequency distributions of duration of relief after using the stimulator and after using the placebo were similar (Fig. 3) no matter how it was tested: the group as a whole (correlated pairs) or according to sites, diagnosis, sex and personality characteristics.

Only 10 patients were lost during the 3-month and 6-month follow-ups. About 87% had 3-month follow-up data, and about 68% had 6-month follow-up data. At the 3-month follow-up, 27 patients were still using the stimulator, and at the 6-month follow-up, 21 patients were still using the stimulator. Eleven of the patients still using the stimulator had reported complete relief of pain during the trial (same sites used for stimulation), but at 3 months this number had decreased to three and then to one at 6 months. No obvious difference in decline in the use of the stimulator was observed

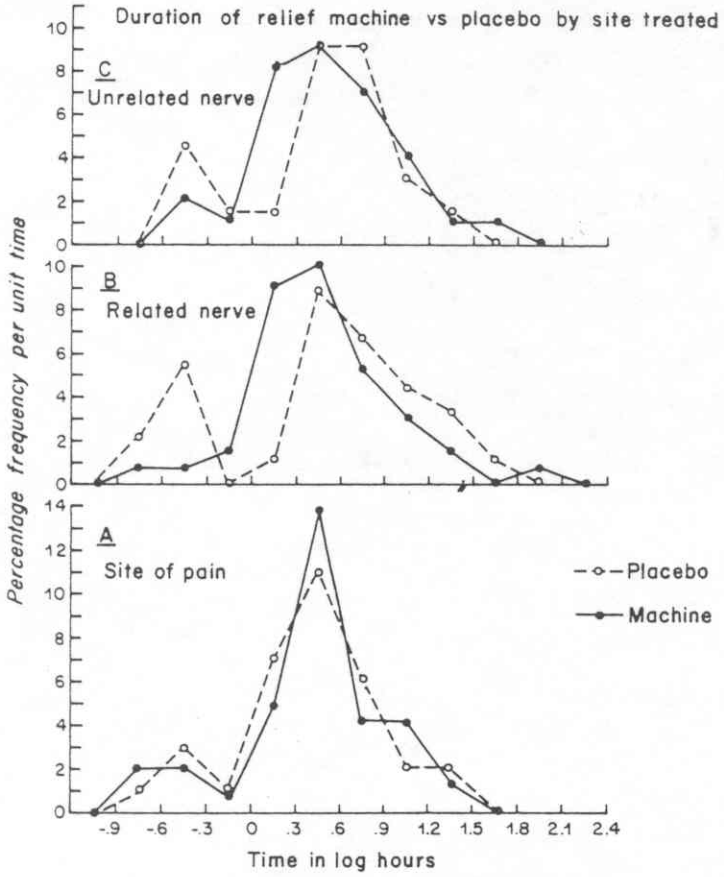

Fig. 3. Frequency distribution of subsequent relief after receiving placebo and after treating with stimulator (machine). Number of patients reporting lasting relief. A: over center of pain: after stimulator 48 and after placebo 33. B: over related nerve: after stimulator 44 and after placebo 30. C: over unrelated nerve: after stimulator 23 and after placebo 22. No significant difference was found between stimulator and placebo responses.

according to diagnosis or sex, but the group of subjects who had depressed MMPI profiles showed the greatest decline in the use of the stimulator (Fig. 4).

DISCUSSION

The use of electrical stimulation was re-awakened by Wall and Sweet [12] when they used it as a source of tactile stimulation to modulate pain according to Melzack and Wall's "gate control theory" [7]. Recently, Kerr [5] has implicated tactile stimulation in his central inhibitory balance theory. Previous reports on the use and effect of transcutaneous electrical stimulation have not been double-blind trials and did not evaluate the placebo effect of TNS [3,4,6,11]. Because a placebo has an analgesic effect [2], it is impor-

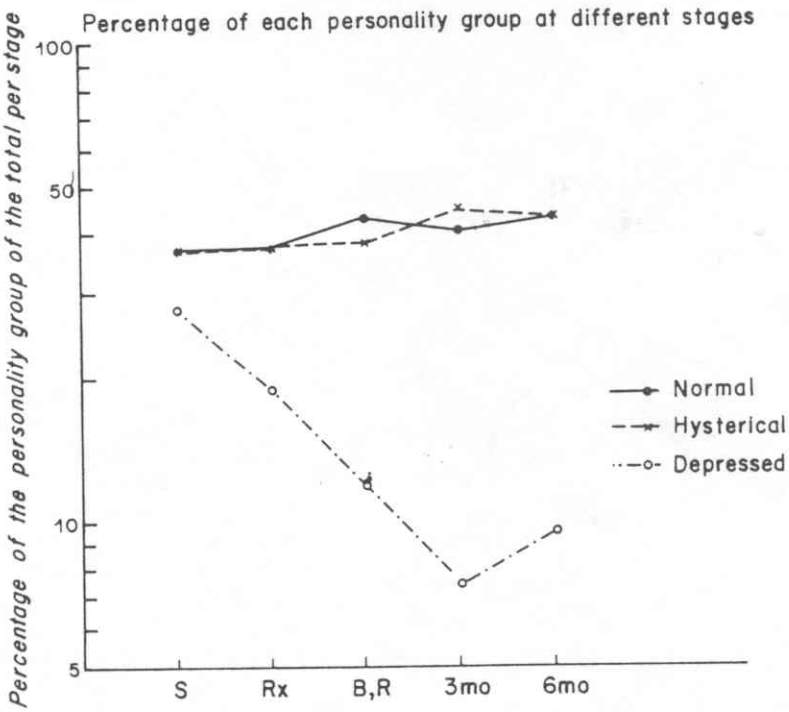

Fig. 4. Comparison among personality groups of the continuing use of stimulator. Stages: S = study trial (N = 93); Rx = stimulator prescribed (N = 48); B,R = known to have bought or rented stimulator and started to use it (N = 44); 3 mo = at 3-month follow-up still using the stimulator (N = 27); 6 mo = at 6-month follow-up still using the stimulator (N = 21).

tant to determine whether the particular device or medication being tested for its analgesic potential has an effect equal to or greater than the placebo. This is of great importance if the new agent has potential complications or is expensive.

The present study revealed that the magnitude of the placebo effect of TNS is similar to that reported in other double-blind trials [2] in which medications were used: an overall effective response of 32% compared with 48% for the stimulator. This type of device would be expected to be most effective when applied over the center of pain (the highest apparent effect) and to be least effective when applied over an area on the body remote from the site of pain. The study revealed that the placebo effect was highest over the center of pain where the apparent effect of the stimulator was the highest but not where the actual effect of the stimulator was the highest, for example, over the related nerve trunk in patients with neuropathies. This kind of placebo effect has been noted in other double-blind trials [2].

The placebo has the same time effect as does the stimulator, and this effect varies according to the site treated. The time effect of a placebo also has been observed in previous double-blind trials [2].

The decline in complete relief obtained reported at follow-up by patients who continued to use the stimulator suggests that the relief of pain rendered by the stimulator is more likely partial rather than complete.

CONCLUSIONS

(1) The placebo stimulator decreased pain in 32% of treatments.

(2) The placebo effect of TNS is similar to the placebo behavior of medications in respect to variations in the apparent effect of the machine and to the time-effect relationship.

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