ELECTRICAL TREATMENT OF ANXIETY STATES

By

J. D. MONTAGU, M.R.C.S., L.R.C.P.

Clinical Research Fellow

Runwell Hospital, Wickford, Essex

and

L. S. DAVIES, M.R.C.S., L.R.C.P.

Deputy Director

Roffey Park Rehabilitation Centre, Horsham, Sussex

DURING the past five years a number of reports have acclaimed Subconvulsive Electrostimulation as a therapeutic measure for the relief of states of anxiety and tension. In general, these accounts have proved unconvincing, since the authors have seldom provided either controls or even details of their results. The report of Hargrove, Bennett and Ford (1953) has been the only exception to both of these criticisms—and the only adverse account. The present investigation was therefore conducted as a "blind" trial in order to provide an unbiassed evaluation of the subject. The series comprised 100 patients, half of whom received the electrical treatment while the other half were subjected to a control procedure. Objective evidence was furnished by psychometric tests. An autonomic test of reputed prognostic significance, and a follow-up study, were also included.

HISTORICAL SURVEY

Hirschfeld (1949), who developed the application of Subconvulsive Electrostimulation under pentothal anaesthesia, first reported, and later confirmed (Hirschfeld, 1950, 1953; Hirschfeld and Bell, 1951), good results with this form of treatment in anxiety-tension states. At the same time, and independently, Alexander (1950) used subconvulsive stimulation through temporo-parietal electrodes as a "countershock" following convulsive treatment with frontal electrodes. By this means he claimed to relieve post-convulsive anxiety. (He also found that the "countershock" may enhance depression, which led him to postulate a reciprocal relationship between depression and anxiety.) Following the initial report of Hirschfeld, L. Alexander (1950) studied the effects of subconvulsive stimulation alone, under pentothal anaesthesia, and he concluded that the outstanding effect was reduction of anxiety, "regardless of the diagnostic category of the patient's illness". Subsequently, however, after working with the autonomic test of Funkenstein *et al.* (1949, 1952), Alexander (1953) restricted the indication for electrostimulation to those patients who have epinephrine-precipitable anxiety, i.e. those in whom a minute intravenous injection of adrenaline precipitates an anxiety attack with symptoms which the patient recognizes as a reproduction of his syndrome.

Good results with electrostimulation in anxiety states have also been reported by Wilcox (1951), Yanof (1952), Paterson and Conachy (1952), Berliner and Schartenberg (1952), and with a somewhat different technique by Berkwitz (1952). The majority of these workers believe that abreactions resulting from the stimulation are prognostically favourable and should be exploited

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(Hirschfeld, 1949, 1950, 1953; Wilcox, 1951, 1953; Berkwitz, 1952; Paterson and Conachy, 1952). However, Berliner and Schartenberg (1952) maintain that they are merely hysterical phenomena which can be prevented entirely by certain simple precautions. L. Alexander (1950, 1953) does not consider that abreactions are necessary for success. He regards electrostimulation not as part of a psychotherapeutic procedure but as a specific physical method of treatment which should be used in conjunction with psychotherapy. This attitude also governed the management of the present series. The only adverse report to date has been that of Hargrove *et al.* (1953), who obtained better results in the treatment of anxiety states by psychotherapy alone than by a combination of psychotherapy and electrostimulation. They concluded that the addition of electrostimulation to the psychotherapeutic regime introduced problems which might even retard recovery. Unfortunately, their method of control did not ensure that the evaluation was unbiassed, since the investigators were aware of the groupings of their patients.

This information may have influenced their psychotherapy as well as their assessment of the results. The only other attempt at a controlled study has been made by Berliner and Schartenberg (1952), who used each patient as his own control by giving a preliminary course of placebo treatments. Their procedure is open to the objection that the control experiments were effected "during the usual period of extensive pretreatment evaluation of the patient". Moreover, they published no details of their results.

It is generally accepted that almost any electrical wave-form may be used for subconvulsive therapy. Hirschfeld (1949, 1950) originally employed the Reiter current, but he later substituted the Brief Stimulus technique with comparable results (Hirschfeld and Bell, 1951; Hirschfeld, 1953). The majority have employed the Reiter current (Alexander, 1950, 1953; Wilcox, 1951; Yanof, 1952; Paterson and Conachy, 1952; Hargrove *et al.*, 1953), but Berliner and Schartenberg (1952) used Brief Stimuli, and Berkwitz (1952) a faradic current, while Paterson and Conachy (1952) have also used A.C. In the present investigation a modification of the Brief Stimulus technique was employed.

Apparatus

The stimulator which was used has been described in detail elsewhere (Montagu, 1955). The current consisted of brief, unidirectional, "square waves", the frequency of which could be varied up to 500 pulses per second. The pulse/interval ratio was fixed, so that any change in repetition rate was accompanied by an inversely proportional change in both pulse duration and interval. In consequence, the average current remained constant, for any given peak current, regardless of the frequency of stimulation. The ratio of the peak current to the average current was 20 : 1, and the maximum peak current obtainable was about 100 mA, with good electrode contacts, corresponding to an average output of 5 mA.

Previous experiments with this apparatus showed that a rise in the frequency of cerebral stimulation from 200 p.p.s. to 500 p.p.s. resulted in a progressive increase in the circulating adrenaline (Montagu, 1955). On the other hand, the motor, sensory, and respiratory effects decreased progressively with increasing frequency. These effects were attributed to a greater sensitivity of the sympathetic centres, and a lesser sensitivity of the other structures, to the higher repetition rates and shorter pulses. Two frequencies were therefore used in the present investigation in order to determine whether there was any therapeutic difference at the opposite ends of the scale. The respective conditions were:

Frequency p.p.s.	Pulse Duration μsec.
200	200
500	80

The electrodes were circular discs, 3 cm. in diameter, which were covered with a layer of chamois leather soaked in saline. In addition, electrode jelly was rubbed into the scalp at the elected sites.

Material

The subjects of this investigation were 100 patients suffering from anxiety states who had been admitted to Roffey Park Rehabilitation Centre. Seventy-five were males and 25 females, with ages ranging from 17 to 58 years. The duration of illness varied from 2 months to 30 years.

The first 50 patients were divided into two equal groups, one of which was treated by stimulation at 500 p.p.s., the other acting as control. These groups will be referred to subsequently as T–500 and C–500 respectively. Two more equal groups were formed from the subsequent 50 cases, one receiving stimulation at 200 p.p.s., the other, again, as a control. These will be known as T–200 and C–200 respectively.

It is impossible to balance groups accurately with respect to the many variants which may influence the course of a neurosis, and it is therefore necessary to select one or two of the more important factors. In the present instance, it was decided to match each pair of groups on the basis of the type of anxiety state, since it was considered that this might be of great prognostic significance. To this end, the patients were subdivided into four types according to the predominant components of their neuroses:

Type 1—Free-floating anxiety.

Type 2—"Conditioned" anxiety, i.e. episodic panic and phobic states occurring in relation to specific situations.

Type 3—Somatic dysfunction.

Type 4—"Displaced" phobic anxiety, e.g. fear of death, doom, or disease.

However, the numbers that could properly be assigned to Type 4 were so small that these were eventually amalgamated with Type 1, so that three categories remained as a basis for matching and for comparison.

No attempt was made to match the groups with respect to age, sex, or duration of illness, since the numbers were fairly large and it was hoped that chance would determine an even distribution. The extent to which this hope was realized is shown in the Table, which demonstrates a greater number of females among the controls. With regard to duration of illness, T–200 constituted a somewhat more chronic population than C–200, but the first pair of groups

Table

Composition of the Experimental Groups

Group	Type			Sex		Age		Duration of Illness		
	1	2	3	M	F	Range	Mean	Less than 10 Months	10 Months to 3½ Years	More than 3½ Years
T–500 ..	7	7	11	20	5	24–56	32·6	6	9	10
C–500 ..	7	7	11	16	9	17–53	34·5	6	9	10
T–200 ..	13	3	9	21	4	20–58	38·5	2	11	12
C–200 ..	13	3	9	18	7	17–58	35·4	4	14	7

was fortuitously matched within the limits of the subdivisions. These were chosen so that in no instance did the duration of illness coincide with a dividing line.

METHODS

One of the investigators (J.D.M.) acted as a "blind" assessor who was unaware of the groupings of the patients. The other investigator was responsible for all the treatments. The psychometric tests were performed by Mr. V. W. Wilson, Psychologist to the Centre.

Patients who were considered suitable for the series were first referred by their physicians to the assessor. Those who were accepted were placed in their appropriate Types (1, 2 or 3) according to the nature of their neuroses, as defined in the preceding section. The series was then managed as follows:

(1) *Groups*

The names of the patients and their Type numbers were given to an independent observer, who divided them into the Treatment and Control groups. Further to avoid prejudice, this division was effected on the basis of alternate selection within each Type, i.e. every alternate Type 1 was allocated to the Treatment group and the same with Types 2 and 3. If, for any reason such as physical illness, a patient dropped out of the series, his place was taken by the next entrant of the same Type.

(2) *Electrical Treatments*

Electrostimulation was performed under pentothal anaesthesia. The dose of barbiturate was adjusted to permit stimulation for five minutes, and with few exceptions 0·5 gm. sufficed. The electrodes were applied bi-temporally about one inch above each ear, and the current was then raised to 4 mA. (80 mA. peaks). This caused initial apnoea (more marked at the lower frequency of stimulation), which usually terminated spontaneously after a few seconds. The current was then maintained at this level for five minutes. In a few cases, a slight reduction in intensity was necessary to promote adequate respiration. Other effects of this current at both high and low frequencies of stimulation have been described elsewhere (Montagu, 1955).

During the first half of the investigation treatments were given on alternate days. This, however, resulted in a reduced rate of discharges, and the programme was subsequently intensified by the institution of daily treatments for five days a week. Twelve treatments were regarded as a standard course but slight variations were not uncommon. At the end of this period the assessor reviewed the cases and referred back to the therapist any patient who, in his opinion, was still improving and might benefit from further treatment.

A total of 631 electrical treatments was given to the 50 patients in the Treatment groups, the distribution being as follows:

Group	Total	Range	Average	
T–500	335	11–18	13·4	12·6
T–200	296	10–12	11·8	

(3) *Control Procedure*

There was no manifest discrimination between the Treatment and the Control groups. All the patients congregated at the same time and place and were called into the Treatment room in random order. To the patients' eyes

the subsequent procedure was the same in every case: the scalp was cleaned, electrode jelly was applied, and an intravenous injection was followed by oblivion. The controls, however, received on an average only 0·25 gm. of pentothal, sufficient to produce anaesthesia for five to ten minutes in the absence of the electric current. Although the staff was adjured to secrecy concerning the nature of the "treatments", it was feared that a nurse might accidentally enlighten any patient whose curiosity became aroused. To minimize the seriousness of such a slip, a further precaution was taken. Sterile distilled water was dispensed under an imaginary trade name, and 0·5 ml. of this was given to each control by subcutaneous injection after the induction of anaesthesia. The nursing staff was told that the object of the investigation was to compare electrostimulation with the new drug, which was purported to give similar results. In theory, therefore, every patient was receiving some treatment. This security measure appears, in retrospect, to have been unnecessary since, as far as is known, the patients never became aware of the existence of different groups. To the very end, subjects who were, in fact, controls periodically attributed their improvement to the electrical treatments.

A total of 622 "treatments" was given to the 50 controls, the distribution being as follows:

Group	Total	Range	Average	
C–500	312	10–16	12·5	12·4
C–200	310	12–16	12·4	

(4) *Clinical Assessments*

Each patient was assessed three times: before and after treatment, and finally after an interval of not less than three months following discharge from hospital. A 4-point scale was used, the grades denoting: symptomless (0), mild (1), moderate (2), and severe neurosis (3).

(a) *Initial*—At the first interview a psychiatric history was taken. Particular attention was then paid to two aspects of the case which were regarded as the principal basis for subsequent intra-individual comparison:

i. Symptomatology. An appraisal was made of the subject's particular symptoms with emphasis on the duration, frequency, and severity of each. In addition, the patient was scored on a standard list of fourteen general symptoms and signs, such as impaired concentration, fatigue, disturbance of sleep rhythm, tremor, etc.

ii. Disability. The details were noted under three headings, relating to work, social adaptation, and home life respectively.

No attempt was made to draw inter-individual comparisons. In every case the patient's condition had been deemed sufficiently severe to warrant admission to hospital, and this fact alone was considered adequate justification for adopting a universal score of 3 at the initial assessment.

(b) *Intermediate*—Each case was reviewed within a week after the end of treatment. At this stage it was generally impossible, by virtue of the individual's removal from the work and home situations, to judge any change in disability. The assessment was therefore based almost entirely on symptoms and attitude of mind. Those who were completely or virtually symptomless and were "rearing to go" scored 0, while others who had come to terms with their symptoms were allotted a 1. Grade 2 implied that the patient was still worried about himself and lacked confidence in his ability to return to his premorbid level of adaptation; 3 denoted no improvement whatever.

(c) *Final*—The follow-up was conducted by questionnaire after an interval of not less than three months following the patient's discharge. At this point the residual disability is both more significant and more objective than the symptomatology as a basis for assessment. Particular attention was therefore paid to the subject's adaptation to the work, social, and home situations, and also to the nature of any treatment received in the interim. The questions were designed to be as factual as possible, and all replies were taken into account in reaching a final score. Regrettably, the groupings had by this time been made known to the assessor owing to the necessity for preparing a preliminary report. The scoring cannot therefore be claimed to be free from prejudice. However, in the last section of the questionnaire the patients were asked to assess themselves as either recovered, much improved, moderately improved, unchanged, or worse, and their replies provided a convenient check.

(5) *Psychometric Tests*

The patients were tested both before and after the treatment period by Mr. V. W. Wilson, who was unaware of their groupings. Two tests were used:

(*a*) Foulds' modification of the Porteus Maze technique (Foulds, 1951). The results of each test were reported as six figures, which denoted the starting time, the tracing time, and the numbers of lifted pencils, wrong directions, crossed lines, and wavy lines respectively.

(*b*) A Word Connection List (Crown, 1952) consisting of fifty stimulus words each of which is associated with a "normal" response word and an "abnormal" response word. The scores denoted the number of "abnormal" responses chosen by the subject.

(6) *Funkenstein's Test*

This test was performed on each individual before the course of treatment in view of Alexander's claim that only those cases who have adrenaline-precipitable anxiety benefit from electrostimulation (Alexander, 1953). The test was repeated again after treatment in order to determine the extent of the correlation between test result and clinical state which has been reported by Funkenstein *et al.* (1951). Only the first half of the test (reaction to adrenaline) was necessary for these purposes, but the second part (reaction to Amechol) was also, in fact, included on every occasion. The method employed was essentially that of Funkenstein *et al.* (1952) with the principal exception that both parts were performed consecutively on the same day. The test was commenced not less than two hours after the previous meal, and the subject was resting completely for half an hour beforehand. No sedation or other medication was permitted during the preceding 24 hours. The subsequent procedure was as follows:

(i) The systolic blood pressure was repeatedly taken until several consecutive readings indicated that a steady resting level had been reached.

(ii) 0·05 mg. of adrenaline (racemic) in 1 ml. of water was injected intravenously, and the systolic blood pressure was followed at intervals of half a minute until it returned to the initial level. Any manifestations of anxiety were noted, and the patient was questioned concerning subjective sensations. A positive reaction was deemed to have occurred if the injection precipitated either a manifest anxiety attack or symptoms which the patient recognized as a reproduction of his syndrome.

(iii) 10 mgm. of Amechol in 1 ml. of water was injected intramuscularly, and the systolic blood pressure was taken at one minute intervals either until

it returned to the pre-injection level or for a maximum of 25 minutes. The patient was again observed and was asked to describe his sensations.

(7) *Psychotherapy*

Each patient received psychotherapy, coupled with occupational therapy, resocialization, and the other ancillary therapies provided by the Centre. The psychotherapy was given by the subject's own physician but not in immediate conjunction with the treatments, so that no attempt was made to foster abreactions for this purpose. On the other hand, drug abreactive techniques were used as aids to exploration, if indicated. The advantages derived from this system were two-fold. The Treatment and Control groups were alike in receiving the benefit of abreactive measures according to individual need. Secondly, and of great importance, it enabled the psychiatrists to be kept in ignorance of the groupings of their patients.

Clinical Results

The progress of each patient was indicated, on a 4-point scale, by three scores, which denoted the clinical state before, immediately after, and again three months after the treatment respectively (*vide supra*). Subtraction of the intermediate and final scores from the initial score yielded two more figures, both also on a 4-point scale, the degrees of which signified: no improvement (0), moderate improvement (1), marked improvement (2), and complete recovery (3). These scores represented the immediate and the follow-up results respectively.

From inspection of these results it appeared that there was nothing to be gained by retaining the 4-point scale of progress. When the grades were combined in pairs to form only two principal categories of response, as shown below, the patients were found to be divided fairly evenly between them and the results were reduced to manageable proportions:

Unimproved	No improvement (0)
	Moderate improvement (1)
Improved	Marked improvement (2)
	Complete recovery (3)

The clinical results, both immediate and follow-up, will be considered in terms of this broad division.

(1) *Immediate Results*

Forty-three of the 100 patients were considered to be improved immediately after the treatment period. When the results were subdivided according to the groupings of the patients, it was found that there was a negligible difference between the Treatment and the Control groups:

	Unimproved	Improved	
T–500	13	12	
C–500	12	13	
T–200	15	10	
C–200	17	8	
T–Total	28	22	(44%)
C–Total	29	21	(42%)

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There was, in fact, a considerably greater difference between the combined "500" groups (50 per cent. improved) and the combined "200" groups (36 per cent. improved) than there was between the totalled Treatment and Control groups. This diminished incidence of therapeutic successes during the second half of the investigation was not statistically significant ($\chi^2=2\cdot0$; $P>0\cdot05$), but it does raise a point of methodological importance, to which reference will be made during the terminal discussion.

(2) *Follow-up Results*

Replies to the follow-up questionnaire were received from 97 of the 100 patients: 42 of them considered themselves to be either recovered or much improved, and these were classed together as "improved"; the remaining 55 stated that they were only moderately improved, the same or worse, and they were regarded as "unimproved". When these categories were analysed in terms of the experimental groups, it was found that the latter were again well matched:

Patients' Assessments

	Unimproved	Improved
T–500	12	13 (52%)
C–500	14	11 (44%)
T–200	16	9 (36%)
C–200	13	9 (41%)
T–Total	28	22 (44%)
C–Total	27	20 (43%)

In a few of these cases, however, there was an obvious discrepancy between the patient's remarks concerning the residual disability and symptoms, on the one hand, and the final self-assessment, on the other. In a few more cases, correspondence with the patient was necessary to obtain further information. Ultimately, the assessor's score differed from the patient's choice of category in 15 cases: 10 patients were considered to be unduly optimistic and were downgraded by the assessor, while in 5 instances the reverse was the case. When these alterations were effected, the results appeared as follows:

Investigator's Assessments

	Unimproved	Improved	
T–500 ..	12	13 (52%)	$\chi^2=4\cdot2$
C–500 ..	19	6 (24%)	$P<0\cdot05$
T–200 ..	17	8 (32%)	$\chi^2<1$
C–200 ..	12	10 (45%)	$P\geqslant0\cdot05$
T–Total ..	29	21 (42%)	$\chi^2<1$
C–Total ..	31	16 (34%)	$P\geqslant0\cdot05$

It is evident from these figures that neither the patients' nor the investigator's assessments showed any significant difference between the totalled Treatment and Control groups. If there was any difference within the series, it must have occurred in relation to the sub-groups. This appears, in fact, to

have happened. According to both patients and assessor, approximately 50 per cent. of Group T–500 were improved at the time of the follow-up. Since this result was the same as the immediate response to the treatment, it is clear that the improvement rate had remained steady, in Group T–500, during the interim period. On the other hand, the corresponding figures for Group C–500 indicate that, according to the assessor, half of the immediate successes in this group subsequently relapsed. When a test of statistical significance is applied to the assessor's follow-up findings in these two groups, the difference is found to be significant at the 5 per cent. level of confidence. It could be deduced from this that stimulation at 500 pulses per second exerted a delayed beneficial effect which prevented the relapses that would otherwise have occurred. That this explanation is unlikely to be correct is evidenced by the fact that the assessor found no such tendency to relapse in the second control group, C–200, in fact rather the reverse. It is interesting that so many members of C–500 should have considered themselves to be improved when their remarks contradicted the fact; C–200, on the other hand, showed a tendency to be pessimistic in their self-assessments. Consequently, when the results in T–500 are compared with those in the totalled Control groups, the significant difference disappears ($\chi^2=2\cdot2$; $P>0\cdot05$).

Psychometric Results

Ninety-six of the 100 patients performed the psychological tests both before and after the treatment period. The results comprised 1,344 scores, of which each subject furnished seven initially and an equal number on retest. From this material two scales of improvement were derived, one for each of the tests. Each scale was then correlated with the immediate clinical response in order to determine the optimal dividing line between "improved" and "unimproved" scores.

(1) *Porteus Mazes*

The method of handling the Maze results was devised with the assistance of Dr. Foulds. Foulds' figures (1951) have shown that individuals suffering from anxiety states have higher scores than normal individuals on all six of the test factors. The difference was statistically significant for starting time, tracing time, lifted pencils and wavy lines; it was not significant for crossed lines and wrong directions, but the trend was nevertheless noted in these components also. For the present purpose, therefore, it was considered justifiable to include all the factors, each with the same sign, in order to obtain a simple index of improvement. This was achieved by giving to each patient a unit score for every factor which was improved on retest. Inspection of the figures then showed that better definition and correlation with the immediate clinical results were obtained when a bonus of one point was given to each patient whose total tracing time (starting time plus tracing time) on retest was 85 per cent. or less of his initial time. The maximum score was therefore 7. Under these conditions, optimal correlation with the clinical results was obtained with a cutting line between 4 and 5 on the psychometric scale. Scores of 5, 6 and 7 were therefore regarded as indicative of improvement, and scores of 4 or less as unimproved according to the test. The association of these categories with the simultaneous clinical results was then found to fall just short of significance at the 1 per cent. level of confidence:

		Clinical		
		Improved	Unimproved	
Psychometric (Mazes)	Improved ..	25	17	$\chi^2=6\cdot55$
	Unimproved ..	18	36	$P<0\cdot02$

(2) *Word Connection List*

The number of "abnormal" responses on retest was calculated as a percentage of the initial score in each case. If a retest result of 70 per cent. or less of the initial score was taken as the criterion of improvement, optimal association with the immediate clinical results was obtained and was found to be significant at better than the 1 per cent. level of confidence:

		Clinical		
		Improved	Unimproved	
Psychometric (Word Connection)	Improved ..	24	15	$\chi^2=7\cdot45$
	Unimproved ..	19	38	$P<0\cdot01$

These associations were held to provide objective support for the clinical assessments. To obtain further confirmation, the test results were studied in relation to the experimental groups, as follows:

	Mazes		Word Connection		
	Improved	Unimproved	Improved	Unimproved	
T–500 ..	11	14	12	13	$\chi^2=1\cdot3$
C–500 ..	11	11	7	15	$P>0\cdot05$
T–200 ..	10	15	10	15	
C–200 ..	10	14	10	14	

With the exception of the Word Connection results in T–500 and C–500, the Treatment and the Control groups were seen to be almost balanced. In the exceptional quarter, there was some difference in favour of the Treatment group, but this difference was not statistically significant.

Although there was a significant association between the results of either test and the clinical findings, it did not necessarily follow that the two tests were in agreement with each other. When their mutual relationship was determined, it was found that there was, in fact, no association between them:

		Word Connection		
		Improved	Unimproved	
Mazes	Improved ..	20	22	$\chi^2=1\cdot5$; $P>0\cdot05$
	Unimproved ..	19	35	

This discovery was rather surprising, particularly since both tests yielded identical results in the second Treatment and Control groups. The conclusion that the tests measured different qualities which were not directly related appears to offer the most likely explanation for the discrepancy.

The lack of correlation between the psychometric tests raised the interesting possibility that one may have had greater prognostic significance than the other. However, the dividing lines between "improved" and "unimproved" scores were derived by comparison with the immediate clinical results, so that, to test this hypothesis, it would be necessary to re-determine the cutting scores on the

basis of correlation with the follow-up results. This procedure would be unlikely to yield substantially different results unless a large number of the patients had remitted or relapsed during the post-treatment period of observation. A survey of the clinical findings showed that 23 of the 100 patients were considered by the assessor to have changed categories at the time of the follow-up: 9 of these were found to be unimproved immediately following the treatment period but were subsequently classified as improved, while the remaining 14 were considered to have relapsed in the interval. When the corresponding test results were noted, it was observed that the Mazes agreed with 10 of the 23 revised assessments, while the Word Connection List confirmed 14 of them. According to the patients' own assessments, on the other hand, 15 of them remitted in the follow-up interval, while a further 15 relapsed. Only 12 of these 30 changes were supported by the Mazes, and only 15 of them by the Word Connection List. The resulting alterations in balance were considered too small to warrant further attention.

Funkenstein Test Results

Ninety-two of the 100 patients were subjected to Funkenstein's Test both before and after the treatment period. The two parts of the test will be considered separately.

A. Reaction to Adrenaline

The first 25 cases were investigated fully, on the basis of both blood pressure response and subjective effects, as previously described. However, no consistent trend could be found in the measurements, nor did there appear to be any relationship between the blood pressure responses, on the one hand, and the psychological effects of the adrenaline or the clinical state of the patient, on the other hand. In subsequent cases, therefore, the test routine was simplified by omission of the blood pressure readings following this injection. The sole criterion of a positive reaction was considered to be the precipitation of a manifest anxiety attack or of symptoms which the patient recognized as a reproduction of his syndrome.

Correlation with Clinical State

The results may be divided into four categories according to whether a positive response was obtained initially, on retest, on neither occasion, or on both. The number of times each of these sequences was encountered is shown in the following table, in which the groups are further subdivided according to the immediate clinical response of the subjects:

Test Result		Clinical		
1st	2nd	Improved	Unimproved	
+	−	16	8	$\chi^2=10{\cdot}98$
+	+	4	18	$P<0{\cdot}001$
−	−	21	22	
−	+	1	2	

It is seen that exactly half of the patients gave a positive response to the first test. Of these, 20 were found to be clinically improved immediately after the treatment period, and in 16 (80 per cent.) of the latter this was accompanied by a negative response to adrenaline on retest. The remaining 26 of the initially-positive cases remained unimproved, and in 18 (69 per cent.) of these the test

result remained positive after the treatment period. It is evident that, in those patients who had adrenaline-precipitable anxiety, there was a positive association between clinical state and test result, which was significant below the 0·1 per cent. level of confidence ($\chi^2=10·98$). This conclusion is in accord with the work of Funkenstein *et al.* (1951).

A negative initial reaction is obviously of no significance in this respect, since the reaction would be expected to remain negative in such cases. In fact, according to the results, three patients developed adrenaline-precipitable anxiety during the treatment period, and one of them was subsequently judged to be improved, but these discrepancies are most likely to be due to wrong interpretation of the precipitated manifestations. If, however, the retest results are considered alone, it is seen that positive reactions were obtained in 25 patients, of whom only 5 were found to be improved.

Prognostic Value

To determine whether the reaction to adrenaline was of any prognostic significance, the results of the first test were studied in relation to the clinical results, both immediate and follow-up, as tabulated below. In the follow-up analysis, two sets of figures are given, of which those in parentheses relate to the patients' own assessments of their progress. Only 89 patients feature in these sections, since 3 of the tested subjects failed to reply to the questionnaire:

First Test	Immediate		Follow-up	
	Improved	Unimproved	Improved	Unimproved
Positive ..	20	26	14 (17)	30 (27)
Negative ..	22	24	19 (22)	26 (23)

Statistical tests are unnecessary in order to determine, from these figures, that there was no significant relationship between autonomic test result and clinical outcome. The patients who had adrenaline-precipitable anxiety stood a similar chance of recovering as those who did not.

B. Reaction to Amechol

The subjective effects of the Amechol were not, unfortunately, noted with any consistency until late in the progress of the investigation. The few observations which were recorded are insufficient to allow any conclusions, and the results have therefore been interpreted entirely on the basis of the blood pressure response. This was regarded as abnormal if there was a fall of more than 10 mm. of mercury which persisted for more than 25 minutes.

According to these criteria, only 10 of the 184 results were abnormal, of which 6 were only just outside the borderline. Three patients gave abnormal responses both before and after the treatment period; two of these patients were clinically unimproved, but the third was found to be improved at the time of the retest. Abnormal responses to the first test alone were encountered in two more cases, one of whom subsequently remitted. A further two patients gave abnormal results only on retest, and both of these remained unimproved.

These numbers are far too small to permit any conclusions, except by virtue of their very paucity. In the light of the work of Funkenstein *et al.* (1949b, 1952), this is an indication that few of the experimental population would have shown a good response to E.C.T. Secondly, with the exception of one abnormal retest response, the results furnish no evidence that the electrostimulation tended to enhance depressive features, and hence the reaction to Amechol, as Alexander (1950, 1953) has reported. The second abnormal response on retest occurred in a control subject.

Discussion

The 50 patients who were treated by electrostimulation showed no significant difference in clinical response from the 50 controls, during the period of observation. Two psychometric tests confirmed the clinical assessments, which also correlated with the reaction to adrenaline (Funkenstein's test) in those patients who had adrenaline-precipitable anxiety. The immediate results, at any rate, cannot have been influenced by prejudice, since the assessor, the psychologist, and the patients' own physicians were none of them aware of the groupings of the patients.

When the sub-groups were taken into account, an exception to this generalization became apparent: the 25 patients who were treated by stimulation at the higher frequency (500 p.p.s.) maintained their improvement rate in the post-treatment period, while the corresponding control group showed a tendency to relapse. However, this difference, which was significant at the 5 per cent. level, was only observed in the assessor's interpretation of the follow-up reports, and it disappeared when the patients chose their own progress categories. Furthermore, the difference was considered to be an artefact because the second control group showed no similar tendency to relapse, in fact rather the reverse. In explanation, therefore, it may have been due to random sampling; but it is also of interest to remember that this was the only point in the investigation at which the assessor was aware of the groupings of the patients.

The discrepancy, in 15 cases, between the patient's choice of progress category, on the one hand, and the assessor's interpretation of the patient's remarks, on the other hand, has a possible explanation apart from prejudice on the part of the assessor. The patient may have been readmitted to hospital, for further treatment, during the period of observation. In this event, the patient was automatically classed as a treatment failure, regardless of subsequent progress. However, this simple explanation is demonstrably unable to account for the conflicting assessments, since a verdict of "unimproved" was returned by each of the 10 subjects who had received further in-patient treatment, including 4 who had undergone leucotomy.

One unexpected discrepancy emerged from the psychological data: there was no agreement between the two psychometric tests, despite the fact that each supported the clinical findings to a similar high degree. The logical conclusion that each test measured different traits which were not themselves directly related appears to offer the most satisfactory explanation for this anomaly. It suggests an interesting field for further studies.

Several investigators have used electrostimulation as an abreactive measure and have claimed that the emotional outbursts are prognostically favourable (Hirschfeld, 1949, 1950, 1953; Wilcox, 1951, 1953; Berkwitz, 1952; Paterson and Conachy, 1952). However, a recent annotation (Anon, 1952) has emphasized that there is no reason to believe that electrical stimuli will prove superior, in this respect, to any of the pharmacological methods. In the present trial, electrostimulation was investigated as a purely physical method of treatment, which was used in conjunction with—but independently of—psychotherapy. No attempt was made to foster abreactions during the treatments. On the other hand, drug abreactive techniques were used as aids to exploration in both Treatment and Control groups, if required. In view of the absence of concern with electro-stimulated abreactions, it is interesting to note that these rarely occurred. This observation confirms that of Berliner and Schartenberg (1952), who took deliberate steps to discourage such abreactions. They concluded that

these outbursts were hysterical elaborations which were motivated by the patient's desire to please and to conform with expectations.

Two possible criticisms of the present trial deserve anticipation. It may be argued that the results were due to the fact that the Controls received better psychotherapy than the Treatment group. This could not have been due to bias on the part of the psychotherapists, since the latter were unaware of the groupings of their patients, but it could still have been caused by accidental mis-matching of the groups with respect to the different physicians. That this was not, in fact, the case is shown by the following figures, which indicate that a good balance was achieved, by chance, in the allocation of the patients:

	Number of Patients		
Physician	Treatment	Control	
A	5	0	
B	9	8	
C	17	19	$\chi^2=5\cdot70$
D	13	17	$P>0\cdot05$
E	6	6	

The results may also be criticized on the grounds that the electric current which was used differed from those that have been employed by other workers. While the authors would agree that this criticism is applicable to the higher frequency of stimulation which was given to the first Treatment group, it is scarcely valid in the case of the second group, who were, for that very reason, treated at the lower frequency of 200 pulses per second. The electrical characteristics in the latter case were similar to those which were used by Hirschfeld and Bell (1951), Berliner and Schartenberg (1952), and Hirschfeld (1953), all of whom claimed good results. Furthermore, the central effects of the current, such as the characteristic tonic contractions, were observed to be the same as those which were reported by these workers, as well as by many others who used different types of current.

One final point, of methodological importance, deserves attention. It has been seen that there was a diminished improvement rate in the last 50 cases of the series, and that this was independent of the groupings of the patients. The difference fell short of significance at the 5 per cent. level of confidence, but two probable contributory causes of the trend are nevertheless evident. In the first half of the investigation, the patients were treated three times a week, which led to a reduced rate of discharges from the Centre and an increase in the waiting list. This state of affairs was remedied in the second half of the investigation by the institution of daily treatments. In consequence, the average course of 12 treatments lasted for only a little over a fortnight instead of for nearly a month. Since the cases were reviewed immediately after the treatment period, the last 50 patients had by then had less time to benefit from their hospitalization. In the second place, it is reasonable to expect that the increased waiting list was reflected, to some extent, in the type of case admitted. In fact, as the Table shows, there was a smaller number of really acute cases, and a higher average age, among the last 50 cases of the series. These factors are considered to be important in the following respect: they emphasize again the necessity, in any controlled investigation, for drawing both experimental subjects and controls from the same, contemporary, population.

Summary

Fifty patients who were suffering from anxiety states were treated by subconvulsive electrostimulation through bi-temporal electrodes under pentothal anaesthesia. In the first 25 of these cases, the frequency of stimulation was 500 pulses per second; the remaining 25 were treated by stimulation at the lower frequency of 200 p.p.s.

Fifty similar cases, likewise divided into two equal groups, acted as controls. They received a course of placebo "treatments", which also included pentothal anaesthesia. No other discrimination was exercised between the Treatment and the Control groups.

Each Treatment group was matched with the corresponding Control group on the basis of the type of anxiety state, according to a simple classification. To prevent prejudice, the classified patients were divided into the Treatment and Control groups by an independent observer and on the basis of alternate selection within each Type.

The average course consisted of 12 treatments or of the same number of control "treatments". In addition, each patient received psychotherapy from his own physician. No attempt was made to foster electrostimulated abreactions for psychotherapeutic purposes.

Two psychometric tests were performed on each patient both before and after the treatment period. The patients were also subjected to Funkenstein's test of autonomic reactivity on both occasions. A follow-up was conducted by questionnaire after an interval of not less than three months following the patient's discharge.

The assessor, the psychologist, and the patients' own physicians were all unaware of the groupings of the patients. Unfortunately, however, these had to be made known to the assessor before the follow-up reports were interpreted. Each patient was therefore asked, in addition, to make a self-assessment, which was used as a check.

The results indicated that:

(1) There was no significant difference in clinical response between the 50 treated cases and the 50 controls, during the period of observation.

(2) At one point there was a significant difference between one Treatment group and the corresponding Control group. However, this difference, which was in favour of the Treatment group, was only observed in the assessor's interpretation of the follow-up reports, and there were reasons for believing that it was unrelated to the treatment.

(3) There was a significant association between each psychometric test and the immediate clinical findings. Furthermore, neither test revealed any difference between the sub-groups. Surprisingly, however, no agreement was found between the two tests, and it was concluded that they probably measured different traits.

(4) The reaction to adrenaline, in Funkenstein's test, was associated very significantly with the clinical findings in those patients who had adrenaline-precipitable anxiety.

(5) The reaction to adrenaline was of no prognostic significance. Patients who had adrenaline-precipitable anxiety stood a similar chance of improving as those who did not.

(6) The reaction to Amechol provided no evidence that electrostimulation enhanced depressive features.

(7) Regardless of their groupings, nearly half of the patients were found to be much improved immediately after the treatment period, and more than a third of them maintained their improvement for at least three months. While these results leave much to be desired, any new form of treatment must be able to better them substantially before it can be considered to be of any therapeutic value.

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