A PSYCHOLOGICAL INVESTIGATION OF STELAZINE AS AN ANTI-PSYCHOTIC AGENT FOR CHRONIC PSYCHOTIC PATIENTS

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CHAPTER I

INTRODUCTION

Trifluoperazine, the generic name for Stelazine, is a new phenothiazine derivative developed for use as an anti-psychotic agent. The earliest research with this drug appeared in the literature in 1958.

On the basis of animal tests, Madgwick, McNeill, and Driver (16) and Bordeleau and Gratton (2) reported that trifluoperazine has nine times the potency of chlorpromazine in blocking a conditioned escape response to harmful stimuli and a greater response specificity than chlorpromazine. Tedeschi, Benigni, Elder, and Yeager (33) compared trifluoperazine with five other phenothiazines in measurement of minimal electroshock seizure thresholds and spontaneous motor activity of mice. The drugs were administered orally to six groups of albino mice with five subjects in each group. The drug treated mice were shocked at 30, 60, 90, 120, 150, and 180 minutes after drug administration; and the character of the seizures was recorded. All of the drugs tested produced significant depression of motor activity; their potency was ranked in the following descending order; trifluoperazine, chlorpromazine, prochlorperazine, promazine, promethazine, and mepazine. Chlorpromazine, promazine, mepazine, and promethazine all produced significant decreases in minimal electroshock seizure thresholds (MET). Trifluoperazine and prochlorperazine did not produce a significant decrease in MET. The data obtained

in this study indicated that a minimal electroshock seizure threshold-lowering action is not a necessary property of effective, potent tranquilizing agents.

Griffiths (7) used a total of 160 wild and domestic rats to measure resistance to stress of forced swimming on Stelazine treatment. He found that none of the differences in swimming times of the domestic rats could be attributed to the effect of Stelazine. Pre-treatment with the drug resulted in significantly longer swimming times, prior to exhaustion, for the wild Norway rats in comparison with rats that did not receive the drug. Griffiths pointed out the need for valid and reliable techniques for quantifying the temperament of the animals in order to have a clearer understanding of the effects of Stelazine treatment on survival times of rats during forced swimming. Wild Cotton rats, group-housed in the laboratory for 30 days and treated with the drug, showed significantly shorter swimming times than untreated subjects, but wild Norway rats, identically treated, showed significantly longer swimming times than the untreated subjects.

Numerous clinical studies using Stelazine have been reported. LeVann (13) used Stelazine for treating behavioral abnormalities in defective children. The drug was given to fourteen idiots, fourteen imbeciles, and five morons. In each of the patients, rage reactions and anti-social behaviors were reduced. It was also found that the drug aided in breaking down communications barriers that oftentimes exist between patients and members of the hospital team responsible for their care.

A study dealing with aggression was conducted by Sexton (28). Trifluoperazine was given to fourteen Negro female schizophrenics for a period of ten weeks. Seven of these patients were in constant restraint

for impulsive violence, destructiveness, and denudativeness. The other seven patients were apathetic and negativistic. Following Stelazine treatment, the seven unruly patients were permanently released from restraint. It was also observed that small doses of Stelazine often produced prompt initial improvement in some of the most disturbed patients.

Petersen (23) found that Stelazine gave relief to a high percentage of depressed patients. He administered the drug to 167 mentally ill women exhibiting marked depression. The depression characteristically "lifted" after the first few days of drug treatment. Paranoid delusions frequently disappeared entirely or were lessened in intensity to such an extent that the patient no longer expressed them spontaneously.

The beneficial effects of Stelazine in the treatment of depressed patients, as Petersen (23) demonstrated, is of tremendous importance in the treatment of mental illness. The characteristic treatment for depression during the last generation has been with electroshock therapy (ECT). MacDonald and Watts (15) found that Stelazine gave better results or results equal to those of ECT or insulin coma treatment (ICT) for treating paranoid schizophrenics as well as patients who were markedly depressed and withdrawn. These investigators employed thirty male chronic paranoid schizophrenics, in an experiment that continued for nine months, as subjects in their evaluation of Stleazine as an anti-psychotic agent. The subjects' duration of illness ranged from two to fourteen years in the mental hospital. Before treatment, only four of the thirty patients were able to adjust to social living in the hospital. After treatment, the other twenty-six patients, who could not adjust satisfactorily, were reduced to nine; twelve patients were able to adjust to social living in the hospital community; four patients were discharged from the hospital

and were able to adjust socially, but were unable to earn a living; and five were discharged from the hospital to engage in full time employment.

Another group of twelve acutely ill psychotics, studied by Rudy, Rinaldi, Costa, Himwich, Tuteur, and Glotzer (25) showed even more improvement than that reported by MacDonald. Eight of these patients showed a marked degree of improvement and six of them were discharged from the hospital and were able to care for themselves on the outside.

Several investigators reported the drug's effectiveness in the treatment of patients in the chronic psychotic state. Tolan and Peppel (34) carried out an eight month investigation of the effects of Stelazine on twelve male and thirty-one female chronic patients. They found the drug to be very effective in the management of chronic catatonic schizophrenia and chronic undifferentiated schizophrenia. These investigators reported that the drug activated lethargic, vegetative patients whose behavior was characterized by psychomotor retardation and apathy.

Twenty males suffering from chronic schizophrenia were treated with Stelazine by Krawieki and Burns (10). Though the duration of Stelazine treatment or hospitalization was not indicated, five of the subjects were discharged to their home communities and full time employment; twelve subjects showed sufficient improvement to permit their transference to open wards; and the other three subjects showed no improvement.

Rudy and his associates (24) used the double blind technique to study two drug effects, trifluoperazine and trifluprom azine. Each drug group was studied with a placebo treated control group. This investigation revealed that trifluoperazine was the more active phenothiazine derivative. Its effective daily dosage (20-60 mg.) produced tranquilization along with marked and varied improvements in alleviating psychotic symptoms.

Kruse (11) tested the efficacy of Stelazine on 110 chronic female schizophrenics over a period of two to eight months. These patients, whose ages averaged 37.4 years, had failed to benefit from any other form of treatment during their average of 5.3 years in the hospital. The most favorable response occurred early in treatment, usually between the first and fourth week. Twenty patients made an excellent response and were discharged from the hospital. Forty-eight patients made a good response and showed alleviation of most of their psychotic symptoms.

Barsa, Saunders, and Kline (1) conducted an experiment with thirty delusional and hallucinated chronic female psychotics. The majority of the patients were withdrawn, flat of affect, preoccupied, and disinterested. At the end of their five to seven month treatment period, one patient was markedly improved and discharged from the hospital. Eight patients were moderately improved though not enough to permit a satisfactory adjustment outside the hospital. Eight patients became more cooperative, and the remaining thirteen patients showed no change.

Side effects have been observed in most studies of the effects of Stelazine upon the human organism. These extra-pyramidal symptoms were manifested most often in the form of Parkinsonism, dystonia, turbulence, akathisia, and restlessness (5). Krawieki and Burns (10) stated that these distressing symptoms resulted in patients' perpetual feelings of restlessness and weakness of the limbs, which was associated with insomnia at night. He found that he could control these symptoms fairly well with administrations of artane. Tolan and Peppel (34) found that extra-pyramidal symptoms are independent of dosage or duration of treatment and that they seem to depend on individual susceptibility to Stelazine. They also found extra-pyramidal syndromes to be more prevalent in females

than males. Davies (4) reported two cases of dystonic reaction in women, ages 18 and 28. The 28 year old patient developed dystonia only six hours after a second 5 mg. dose of Stelazine. The 18 year old patient, also had a dystonic reaction following a second 5 mg. dose of the drug. When dosage was stopped, symptoms subsided within six hours in each case. Goldman (6) reported Parkinsonism occurring in not less than 35 percent of the patients treated with Stelazine for one month or more. Kinross-Wright (9) reported that Parkinsonism occurred twice as frequently in women than men under treatment with Stelazine. Nine cases of Parkinsonism developed in a group of twenty chronic schizophrenic males in an investigation by Markey (18), but all the side effects were reversible within a few days when medication was stopped or when dosage was sufficiently reduced.

The Shipley-Hartford Intelligence Scale (30) and the Minnesota Multiphasic Personality Inventory (MMPI) (8) were both used in a study of the short term effects of chlorpromazine on psychiatric patients. (35). The Shipley-Hartford was used as an estimate of the intelligence of acute psychotic female patients newly admitted to the mental hospital. On the basis of intelligence, fifty-nine patients were given drug and placebo treatments for a period of one week. The MMPI was administered before and after treatment to measure response changes. All nine clinical scales and the three validity scales were administered on pre and post treatment trials. Test-retest reliability coefficients, based on thirty-one cases, were computed for all twelve scales of the inventory. Reliability coefficients of .86 were reported for scales lie (L) and psychasthenia (Pt), but coefficients between .75 and .79 were reported for validity (F), hypochondriasis (Hs), and schizophrenia (Sc) scales.

Coefficients for the remaining seven scales were less than .75.

Schmidt (27) administered the MMPI to 121 maladjusted army personnel at a United States Army base hospital and compared the test results with the diagnostic impressions of the army base psychiatrist. The testee was interviewed in a standard diagnostic interview when the psychiatrist had no knowledge of the patient's test results. The principle investigator found the MMPI to make statistically significant distinctions between neurotic and psychotic soldiers. Modlin (21) found that neuroticism was present when three scale scores, hypochondriasis (Hs), depression (D), and hysteria (Hy) were elevated on a given test profile. In contrast to this "neurotic triad," he further identified the "psychotic triad" by the elevated scores on the paranoia (Pa), psychasthenia (Pt), and schizophrenia (Sc) scales. His comparison of neurotic and psychotic scores provide a noteworthy clinical differentiation between neurotic and psychotic patients.

In an investigation of the short term effects of chlorpromazine, Winter and Frederickson (35) used the double blind technique with drug and placebo groups. The Shipley-Hartford Intelligence Scale was employed for matching the groups on intelligence and the MMPI was administered on pre-and post-treatment trials. A statistically significant change was found on MMPI performance. Steiper and Weiner (31) used the Shipley-Hartford and the MMPI to study the relationship between test scores and time spent in psychotherapy. These investigators found that length of time in psychotherapy did not correlate with improvement on test scores. Shipley and Burlingame (29, 30) standardized the test on 171 chronic psychotic state hospital cases, 203 neurotic and psychotic private hospital cases, and 1046 normals. They found that the

ratio of abstract thinking ability to vocabulary level was an adequate index to degree of intellectual impairment. Reliability coefficients, based on 322 army recruits, were .87 for vocabulary, .89 for abstract reasoning, and .92 for the combined scales.

The HAS consists of three groups of scores that refer to different types of behavior. The Group I score relates to communication and interpersonal relations; the Group II score relates to care of self and social responsibility; and the Group III score relates to work, activities, and recreation (20). Group scores are the basic units of measurement on the HAS. Lorr (14) reported that the Hospital Adjustment Scale (HAS) is an ingenious, carefully constructed device for evaluating the behavior of hospital patients. He found that it distinguished between patients showing improvement in adjustment and approaching discharge and the disturbed or chronic hospital residents. The procedure for completing this rating scale typically requires from 10 to 15 minutes and can be done by the ward nurse who is best acquainted with the patients (19). Stilson (32) found a reliability of .79 for the HAS when test-retest scores were obtained two weeks apart by student nurse raters.

The Malamud-Sands Psychiatric Rating Scale (17) provides a single score as an index to degree of pathology. To test the validity of this rating scale, six pairs of psychiatrists did several ratings on a total of 26 patients. On 180 paired ratings, the correlation coefficient for the six pairs of raters was .92.

CHAPTER II

STATEMENT OF PROBLEM

Previous procedures described in the literature concerned with evaluating the influence of Stelazine on the behavior of psychotics have been restricted to generalizations relative to the employment of subjective measures to determine the amount of improvement shown by patients. Hospital patients who are treated, discharged, and not re-admitted provide the best criterion for judging the effectiveness of the drug. However, when patients are judged to be markedly improved, somewhat improved, or mildly regressed, with no further quantification, the true effects of the drug treatment are clouded.

There appears to be a critical need for the development of quantitative methods in determining the influence of tranquilizing drugs on behaviors of organisms. This need has been partially alleviated by the study of Tedeschi, et al. (33) concerned with the effects of Stelazine on electroconvulsive shock thresholds and spontaneous motor activity of mice. Griffiths (7) has also presented quantitative data concerned with the effects of Stelazine on resistance to exhaustion of forced swimming of wild and domestic rats. Madgwick (16) found a significant increase in speed of performance on the Modified Peg Board Test of motor speed and a significant increase in scores on the Knox Cube Attention level test in a study of the effects of Stelazine on chronic psychotic patients. Lehman and Knight (12) have reported empirical measures on a

series of psychophysiological tests administered to normal humans prior to and following a single treatment with Stelazine.

In the present study, four psychological tests were given to two groups of chronic psychotics; one group maintained on Stelazine, the other on placebo. The duration of the treatments was 66 days and the problem was to determine whether the drug treated group would show significant improvement in hospital adjustment as measured by the Hospital Adjustment Scale (14, 19, 20, 32), in personality organization as measured by the Malamud-Sands Psychiatric Rating Scale (17) and the Minnesota Multiphasic Personality Inventory (8, 21, 27), and in intelligence in terms of the Shipley-Hartford Intelligence Scale (29, 30).

CHAPTER III

METHODS AND PROCEDURE

A. General Methodology

The present study was conducted in order to ascertain whether patients treated with Stelazine for a period of 66 days would improve significantly over a matched group of patients treated with a placebo for the same period of time.

A significant improvement is defined as a difference at the 5 percent level of confidence or less between the post-treatment tests and ratings of the two treatment groups. This level of confidence was arbitrarily selected as the criterion for rejecting the null hypothesis of no difference between the groups.

Independent Variable

Stelazine was administered orally each day to the patients in the Experimental Group throughout the duration of the study. The dosage was carefully titrated for each patient individually by the medical advisor in order to achieve maximum benefit with the lowest possible dosage.

Dependent Variables

Four dependent variables were measured in the study. Adjustment to hospital living conditions, observed in the patients' overt behavior, was rated at three periods on the Hospital Adjustment Scale. Changes in

intellectual functioning were measured immediately before and immediately after Stelazine therapy by the Shipley-Hartford Intelligence Scale. Fluctuations in personality organization were rated at three periods on the Malamud-Sands Psychiatric Rating Scale. The Minnesota Multiphasic Personality Inventory (MMPI) was also administered before and after drug therapy to reflect changes in personality structure. Greater pathology is indicated by higher scores on the Malamud-Sands Psychiatric Rating Scale and the MMPI, and by lower scores on the Hospital Adjustment Scale and Shipley-Hartford Intelligence Scale.

B. Subjects

A homogeneous sample of patients was selected from the female chronic wards at the Eastern Oklahoma State Hospital. The sample was divided into two groups of 24 patients by random assignment of patients to Experimental and Control Groups.

Criteria for Selection

1. Age. The age range of the subjects in the study was from thirty to forty nine years. The mean age for these patients was 41.5 years.

2. Sex. Only female patients were used as subjects.

3. Physical Health. Subjects in the present investigation were free from neurological impairment and relatively free from other chronic or acute physical disorders. Mental defectives and patients suffering from organic involvement in their psychosis were not included in the study.

4. Functional Psychotic Disorders, Chronic. Subjects were patients who had been diagnosed as chronic psychotics and who had been retained on a chronic ward for fifteen months or longer. The average length of hospitalization for all subjects was 8.6 years.

5. Behavior. The subjects were withdrawn, apathetic, and lethargic, and were mostly "sitters" on the wards. This group of patients had no work assignments.

6. Preselection Testing. Only those patients who could demonstrate the ability to read, understand, and make decisions on a group of 30 statements were considered for this study.

C. Procedure

Preselection Interviews

A homogeneous sample of 48 patients was selected as subjects from all the chronic psychotic female wards, located in the same building, at the Eastern State Hospital. All the patients on the chronic wards who met the first four criteria for selection were given an intensive diagnostic interview. The interviews were conducted in the same manner as regular patient staff meetings. Each patient's hospital record was carefully reviewed before the patient was called to appear. The persons taking part in the interviews were a psychiatrist of diplomate status, the ward physician, a registered nurse who had completed psychiatric training, and a clinical psychologist. Each person assisting with the interviews had observed the patients' behaviors in different situations, which were usually unknown to the other three persons on the interviewing team. Each person, therefore, was able to make contributions to the interviews by being in possession of information that was unique to his own professional role. The purpose of the preselection interviews was to select only those patients who met the fifth criterion for selection. About 160 patients were interviewed on the same day.

Preselection Testing

Sixty-nine patients, who met the first five criteria were administered a preselection test. The test was made up of 30 items from the MMPI which were statements of behavior and attitudes that the patients were required to answer as either true or false as it applied to themselves. The purpose of the preselection test was to eliminate the patients who would be unable to participate in periodic psychological testing. Twenty-one patients were eliminated because of their inability to read, understand the meaning of the statements, or because of their inability to determine whether the statements had reference to their own behavior. Following this final step in the preselection procedure, the remaining 48 patients were taken off of all tranquilizer medication for a period of 21 days prior to the beginning of their Stelazine therapy.

Random Selection of Experimental and Control Groups

The random selection of Experimental and Control subjects was achieved by the following method: first, the names of all 48 patients were typed on small cards of one and one-half inches in length and one inch in width. The diagnostic classification was typed directly beneath the patient's name. Second, the cards were placed in a small box which was eight inches long, four inches wide, and three inches deep and the box was shaken for thorough mixing of the cards. Third, a neutral person, who was blindfolded, drew one card at a time from the box and a secretary recorded the names alternately on the Experimental and Control lists. The remaining cards in the box were thoroughly mixed following each draw. Since Stelazine is purportedly most effective with patients of the Schizophrenic Reaction, Catatonic Type, randomization was done first

with patients of that classification. This stratified randomization provided each group with an equal representation of Catatonic subjects. The remaining names were assigned in the same random fashion. The identity of the Experimental and Control subjects was known only by the medical advisor and the secretary who typed the lists. The Experimental Group received Stelazine tablets daily and the Control Group received daily administrations of the placebo throughout the entire study.

Group Psychotherapy

The subjects in this investigation also participated in group psychotherapy throughout the period of Stelazine therapy. The combined treatment groups were divided into four equal therapy groups. The same random procedure of assigning subjects to Experimental and Control Groups was used in assigning subjects to the four therapy groups. However, three changes were made in group therapy assignments to provide greater homogeneity of the individual groups and to facilitate communicative interaction within the groups. Each therapy group met one session per week on their scheduled day. Group therapy was scheduled on Tuesday, Wednesday, Thursday, and Friday; the therapy sessions began promptly at 8:15 A. M. and ended promptly at 9:15 A. M.

An experienced group therapy observer met each therapy session and took detailed notes to provide a "running account" of each session. The primary role of the observer was that of an unobtrusive secretary, who refrained from participating in any form of group interaction. After each therapy session, the observer and therapist met for approximately 30 minutes in order to evaluate and summarize the data. The summaries of each meeting were dictated and typed for a permanent record.

The role of the therapist in the group sessions was primarily non-directive and supportive. The patients instead of the therapist played the central role in their attempts to achieve resolution to emotional disturbances. The therapist refrained from making any suggestions to the patients about the nature of their problems, and no advice was given or directive methods employed to help patients with emotional problems; however, patients were encouraged to talk out problems of a conflicting nature.

Testing Schedule and Test Instruments

The four tests measuring the dependent variables were given in the following order: the first testing was completed two days prior to the beginning of Stelazine therapy and three days prior to the beginning of group therapy. Each subject was rated on the Hospital Adjustment Scale by the ward nurse and attendants; the Shipley-Hartford Intelligence Scale and the MMPI were administered during two testing periods to 24 subjects at each period; and ratings on all the subjects were made by two staff physicians using the Malamud-Sands Psychiatric Rating Scale. The first testing was completed in a period of two days and these results supplied the necessary pre-treatment test data for the study. All the subjects were rated again on the Hospital Adjustment Scale and the Malamud-Sands Psychiatric Rating Scale after the first 21 days of drug therapy in order to determine the extent of the quick-acting aspects of Stelazine. The time required for the completion of these ratings was two days. When the study was terminated after a period of 66 days, all four measuring instruments were again employed over another two day period to provide the necessary post-treatment test data for the study. The procedure used for testing and completion of rating scales was held constant

throughout the study; the same persons used the same measuring instruments after each appropriate time interval.

D. Experimental Controls

Two Matched Groups of Subjects

Two matched groups of subjects were obtained by careful selection of subjects on the basis of possession of characteristics that are similar and equal for the purposes of this study. Matched groups were used in an attempt to exclude all extraneous variables possible in determining the relationship between independent and dependent variables.

Previous Medication

The medical advisor for the project gave written orders to the ward nurse for all project patients' tranquilizer medication to be discontinued for the period of 21 days prior to Stelazine therapy. The only medicines permitted were aspirin tablets and laxatives. These orders were given as an effort to control for the influence of prior tranquilizer medication.

Drug and No Drug Treatments

The method of randomization assured the probability of .50 for the placement of each patient in the drug or no drug treatment group.

Double Blind Method

Through the medical advisor's refusal to disclose the identity of Experimental or Control subjects to any person, neither subjects nor persons assisting with the project could determine with certainty the

identity of drug or no drug patients. The subjects in the study were told that the drug has differential effects upon people.

The double blind method was successful in eliminating biasing effects that might have occurred in rating scale judgements as well as patient-therapist relationships in group therapy.

Control of Dosage

Written orders were given by the medical advisor to the ward nurse before dosage was increased or decreased for any subject. This control of medication ruled out the potential variable of over dosage and under dosage. When subjects refused the medicine, it was given in liquid form in fruit juice or by intramuscular injection. These controls of dosage were an aid in achieving the maximum therapeutic effects of Stelazine.

Three Testing Trials

The three testing trials in the study, which were given before treatment, after 21 days of treatment, and after 66 days of treatment, provided methods of determining the degree of changes taking place after those intervals of time.

Group Therapy Controls

(a) The Role of the Therapist. The non-directive method was employed and held relatively constant for all four therapy groups. By keeping therapy on the "client centered" level, the opportunity was made available for subjects to ventilate their feelings and verbalize anxieties that were apparently elevated as a function of the energizing effects of Stelazine. Adhering to this method of psychotherapy also placed

controls on the therapist and helped to eliminate the factor of bias.

(b) The Role of the Observer. The role of the observer in group therapy was that of a secretary who took detailed notes on subjects' verbalizations. Small group interactions were also noted.

CHAPTER IV

RESULTS

In order to study the psychological effects of Stelazine on chronic psychotic patients after specified periods of treatment, the standard errors of differences between means were computed for each of the three testing trials. The mean basic unit scores, divided by a constant of 10 and rounded to the nearest whole number, are presented in Table I.

TABLE I

AVERAGE HOSPITAL ADJUSTMENT SCALE SCORES OF STELAZINE AND PLACEBO TREATED PATIENTS

Trials	Treatments		Average
	Placebo	Stelazine	
I	7.6	7.5*	7.5
II	7.7	8.5	8.2
III	7.6	8.8*	8.3
Average	7.7	8.3	

* Necessary difference between trials I and III = 1.02 ($p < .05$).

A significant difference between scores made on trial I (prior to drug treatment) and those shown for trial III (after drug treatment), for the Stelazine treated subjects, indicates that the drug had a beneficial

effect on the behavior of these chronic psychotic patients ($p < .05$). However, a comparison of scores obtained during the pre-treatment period with those obtained after 21 days of drug treatment, indicated that the difference in scores merely approached significance for the Stelazine patients on short term treatment.

Mean Hospital Adjustment Scale scores, for chronic psychotic patients on Stelazine and placebo treatments, are presented in Figure 1, which shows the changes in behavior that were observable prior to treatment, during treatment, and following treatment. A statistical analysis of the Hospital Adjustment Scale scores obtained by the subjects in both treatment groups, appears in Table I of Appendix A. This analysis, based on scores obtained on trials II and III (second and third administrations of the test), demonstrated a significant difference in favor of the Stelazine treated patients after 66 days of drug treatment ($F = 4.40$, $p < .05$).

The mean scores for trials I, II, and III on the Malamud-Sands Psychiatric Rating Scale are presented in Table II. An analysis of the treatment data (trials II and III) appears in Table II of Appendix B, which shows that the Stelazine treated patients failed to demonstrate significant improvement over the placebo treated patients on ratings of personality functions ($F = 1.03$, $p > .05$). The mean Malamud-Sands Psychiatric Rating Scale scores for trials I, II, and III are presented for Stelazine and placebo treated patients in Figure 2, which shows the placebo treated patients to be slightly superior to the drug treated patients on trial III. The analysis indicated that the observed difference was not statistically significant. The sums of scores and means for the Stelazine and placebo patients on fifteen functions of behavior

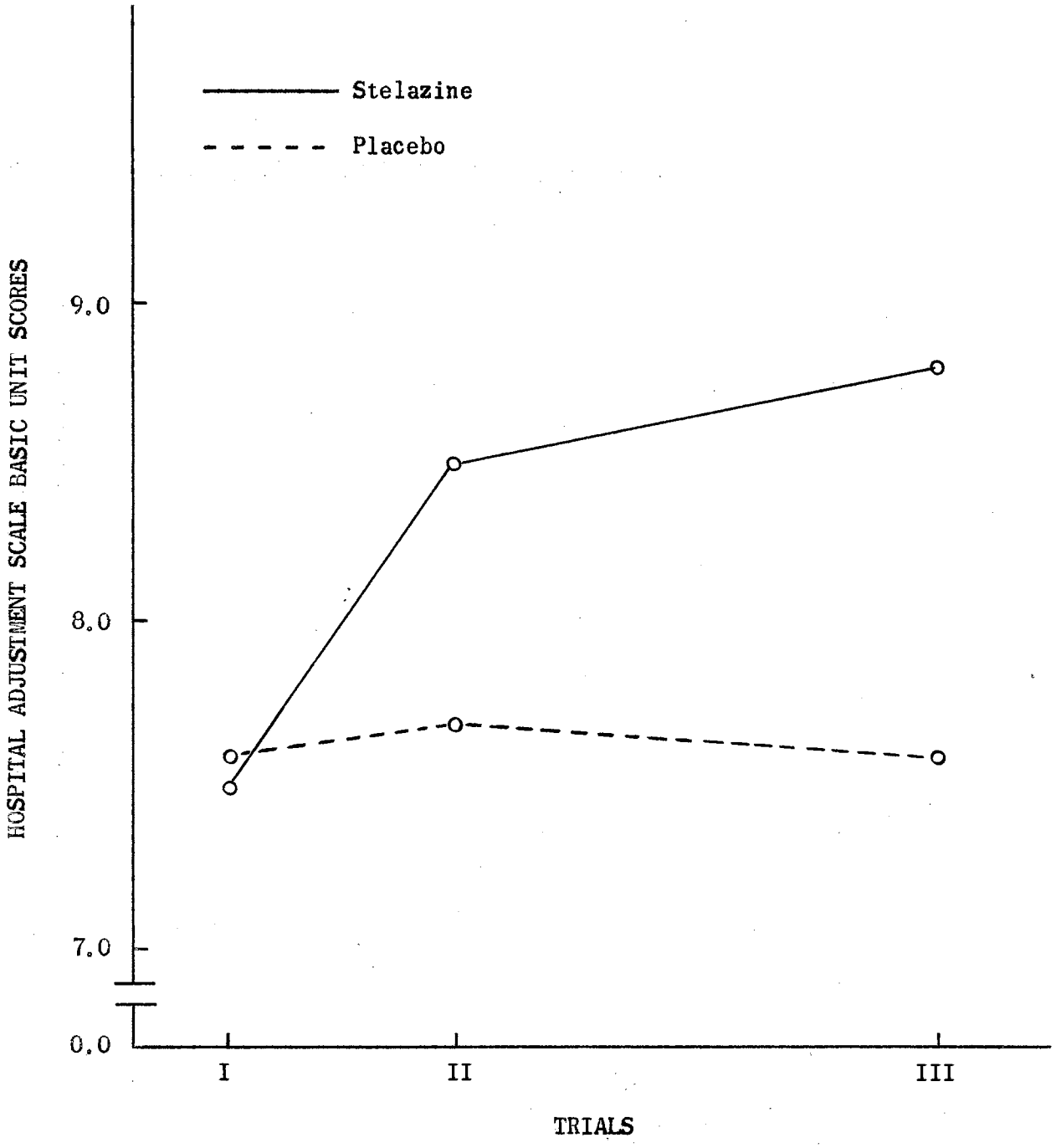

Figure 1. Mean Hospital Adjustment Scale basic unit scores for chronic psychotic patients on Stelazine and placebo treatments. Trial I is a pre-treatment rating; trials II and III were administered after 21 and 66 days of treatment, respectively.

rated on the Malamud-Sands Psychiatric Rating Scale for trial III are presented in Table III. Lower scores, indicating less pathology for the placebo patients, were found on the following functions: motor activity, socialization, speech, mood, affect, and feeling.

TABLE II

EFFECTS OF STELAZINE ON MEAN MALAMUD-SANDS PSYCHIATRIC RATING SCALE SCORES

Trials	Treatment Groups		
	Experimental	Control	Average
Pre-Treatment Trial I scores	16.12	16.57	16.33
During Treatment Trial II scores	15.62	15.28	15.47
Post-Treatment Trial III scores	15.31	12.57	14.03
Average	15.68	14.80	14.03

Neurotic and psychotic triad difference standard scores between the pre- and post-treatment testing of Stelazine and placebo treated patients were obtained from the Minnesota Multiphasic Personality Inventory (MMPI). The sums of the differences of standard scores for hypochondriasis (Hs), depression (D), and hysteria (Hy) of the neurotic triad are presented for the drug and control groups in Table IV. An analysis of the difference scores on the neurotic triad scales which appears in Table III of Appendix C, fails to show any superiority for Stelazine treated subjects on these measures.

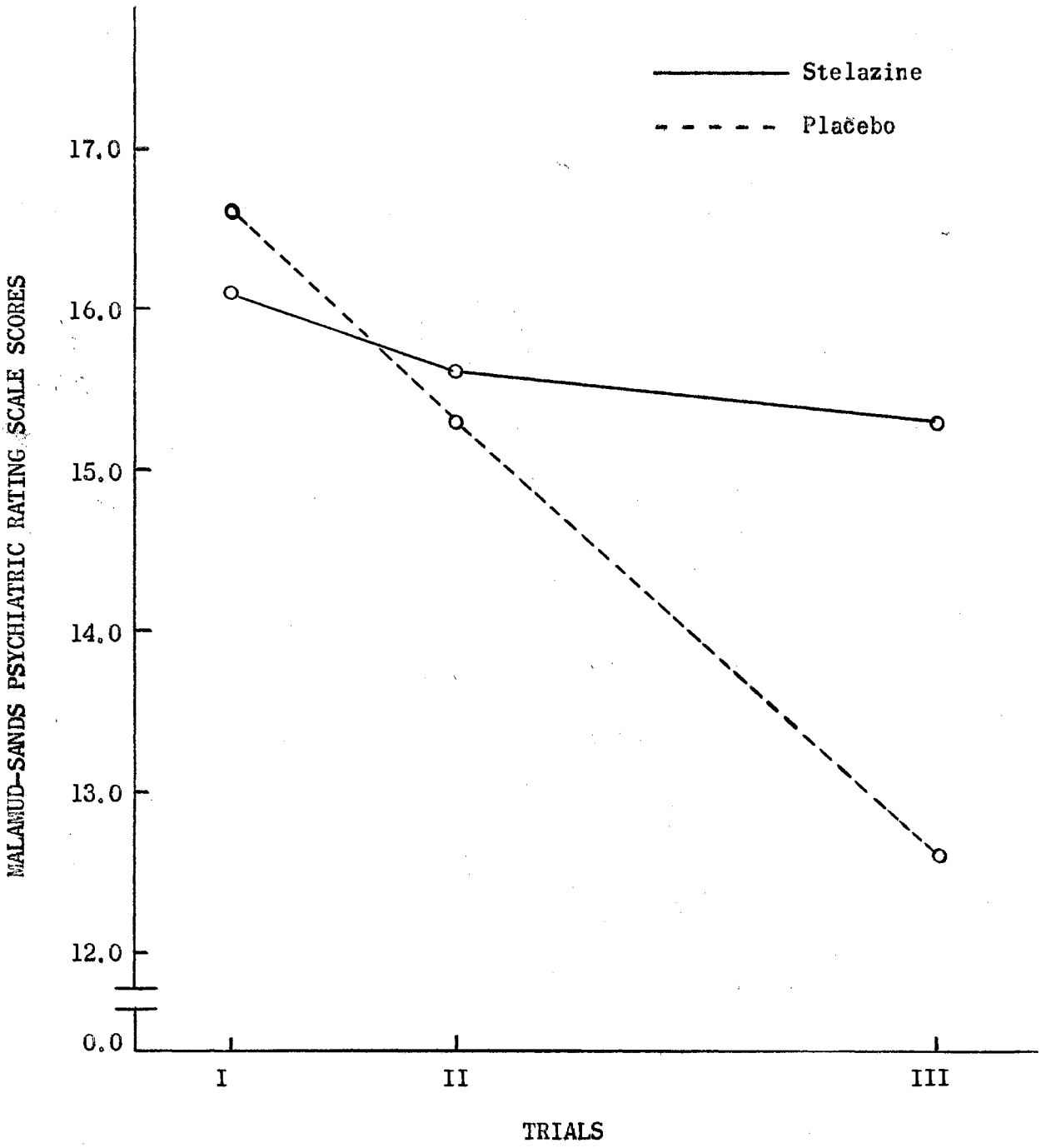

Figure 2. Mean Malamud-Sands Psychiatric Rating Scale scores for chronic psychotic patients on Stelazine and placebo treatments. Trial I is a pre-treatment rating; trials II and III were administered after 21 and 66 days of treatment, respectively.

TABLE III

SUMS OF SCORES AND MEANS FOR 15 FUNCTIONS OF BEHAVIOR ON THE MALAMUD-SANDS PSYCHIATRIC RATING SCALE FOR TRIAL III

Function	Stelazine Patients	Placebo Patients
Appearance	4	6
Motor Activity	15	8
Mimetic Expression	12	9
Responsibity	9	9
Hostility Reaction	7	6
Socialization	18	9
Attention	6	6
Speech	13	4
Mood	13	7
Affect	19	10
Feeling	20	6
Perception	11	6
Thought Processes	18	18
Subjective Reorganization	20	20
Insight	60	52
Sum	245	176
Mean	15.31	12.57

TABLE IV

NEUROTIC TRIAD DIFFERENCE SCORES BETWEEN PRE-AND POST-TREATMENT TESTING ON THE MMPI (PLUS A CONSTANT OF 8.00)

Stelazine Group (N = 16)	Placebo Group (N = 14)
10.33	.34
8.33	12.00
8.66	7.67
5.33	5.67
14.37	13.00
11.00	10.00
11.33	9.33
7.66	3.33
3.00	10.33
10.33	8.66
6.00	15.00
7.14	8.33
10.34	2.34
6.67	10.66
9.00	
6.67	Sum = 116.66
Sum = 136.13	

The sums of the differences of standard scores for paranoia (Pa), psychasthenia (Pt), and schizophrenia (Sc) of the psychotic triad are presented for the Stelazine and placebo treated patients in Table V. The analysis of the difference scores on the psychotic triad scales appears in Table IV of Appendix C, and fails to indicate any significant effect of the drug on these measures of behavior.

Differences between pre- and post-treatment raw scores on the Shipley-Hartford Intelligence Scale vocabulary and abstract reasoning tests are presented in Tables VI and VII. An analysis of the pre- and post-treatment vocabulary difference scores shown in Table V of Appendix D indicates that the Stelazine treated patients failed to show a statistically significant improvement over the placebo treated patients. The analysis of pre- and post-treatment abstract reasoning difference scores, presented in Table VI of Appendix D, shows that the drug treated group failed to demonstrate a significant improvement over the placebo treated group.

TABLE V

PSYCHOTIC TRIAD DIFFERENCE SCORES BETWEEN PRE- AND POST-TREATMENT TESTING ON THE MMPI (PLUS A CONSTANT OF 25.00)

Stelazine Group (N = 16)	Placebo Group (N = 14)
37.00	.66
20.67	24.00
23.00	32.33
15.33	10.67
19.00	28.00
23.00	25.00
26.67	28.34
29.00	21.67
25.00	26.66
26.67	29.34
13.67	33.34
22.33	29.00
38.34	24.00
22.00	26.00
22.00	
25.00	Sum = 339.01
Sum = 388.68	

TABLE VI

VOCABULARY DIFFERENCES IN RAW SCORES ON THE SHIPLEY-HARTFORD INTELLIGENCE SCALE (PLUS A CONSTANT OF 8.00)

Stelazine Group (N = 16)	Placebo Group (N = 14)
10	9
15	8
7	6
0	6
7	10
13	9
9	6
10	9
6	3
10	9
12	12
7	12
11	10
14	10
17	
7	Sum = 119
Sum = 155	

TABLE VII

ABSTRACT REASONING DIFFERENCES IN RAW SCORES ON THE SHIPLEY-HARTFORD INTELLIGENCE SCALE (PLUS A CONSTANT OF 2.00)

Stelazine Group (N = 16)	Placebo Group (N = 14)
6	6
2	4
2	2
2	2
2	8
8	6
2	2
4	2
4	12
6	16
2	2
4	4
4	0
2	6
14	
12	Sum = 72
Sum = 76	

CHAPTER V

DISCUSSION

From the total group of 48 subjects participating at the start of the present study, 14 were eliminated due to additional medications introduced by the medical department. Four other subjects were eliminated prior to the beginning of the treatment period because of behavioral disturbances that prevented their participation.

It was supposed that the residual effects of previous medication, administered over a long period of time to the patients prior to their participation as subjects in this study, rendered it difficult for some of the patients to be maintained on Stelazine alone and even more difficult for others to be maintained on a placebo. The fact that more of the control than experimental subjects were lost from the study seems to infer that Stelazine has tranquilizing as well as stimulating properties.

Statistical analyses of test results obtained in the present study indicate that Stelazine is a very effective agent for the treatment of chronic psychotics, when administered to markedly withdrawn, lethargic, and apathetic patients. A statistically significant difference ($p < .05$) in favor of the Stelazine group on Hospital Adjustment Scale scores indicated that the drug treated patients were responding to the environment and social milieu of the hospital.

By the end of the first two weeks in the study, the occupational

therapist had assigned work duties to all of the subjects in the project. Five Stelazine patients did not continue with their work assignments, because two of them were discharged to their homes and self supporting employment, one patient was relieved from work duties because of Parkinsonism, one patient fell down stairs and fractured a femur, and the other drug treated patient became disturbed and could not continue with her work assignment. Five placebo treated patients failed to continue their work assignments because four patients were too disturbed and disruptive to do the work, and one placebo treated patient was transferred to a nursing home, which is a type of "half-way house" to being discharged. It is also noted that none of the patients who required extraneous medication were considered for discharge.

The chief value of the Malamud-Sands Psychiatric Rating Scale in the present study was demonstrated by its use in detecting and quantifying the excitatory effects of Stelazine in the drug treated subjects. The use of this scale would appear to impose a bias against the effectiveness of Stelazine, since the energizing effects of the drug elevated scores of some of the scales of behavior functions. However, this instrument proved to be valid for discriminating between patients who were drug treated and those who were treated with the placebo. Some of the elevated scores for the drug treated patients were found on functions of motor activity, which showed restlessness or excitability; socialization, which was observed to be outreaching or meddlesome; speech, which was usually overproductive; mood, which appeared to be enthusiastic or euphoric; and feeling, which was usually tense or anxious.

Extra-pyradmidal symptoms, or side effects, were also reported from the psychiatric interviews. There appeared to be three unmistakable

cases of Parkinsonism. The most interesting case was one patient who appeared to have all the symptoms of incipient Parkinsons Disease, but this patient was a subject in the placebo treatment group. She referred to her symptoms as being "like those of the other girls." Her symptoms disappeared when the Stelazine dosage of the Parkinsonism cases was reduced.

Stelazine appears to be a very potent and quick acting agent for the treatment of chronic psychotics. In only 66 days of Stelazine treatment, chronic psychotic patients, who had averaged over 8 years in the mental hospital, made a statistically significant improvement in adjustment to the hospital living conditions; but when differences in Hospital Adjustment Scale scores obtained prior to drug treatment and after 21 days of drug treatment were analyzed, the degree of improvement failed to reach significance by only .02. This could have been a result in the method of handling basic unit scores, which were divided by a constant of 10 and rounded to the nearest whole number. Some precision was undoubtedly lost with this method.

The differences between pre-and post-testing scores obtained on the Minnesota Multiphasic Personality Inventory were non-significant for the experimental group and for the control group, when raw scale scores were converted into standard scores and grouped on the neurotic triad (scales Hs, D, and Hy), and on psychotic triad (scales Pa, Pt, and Sc). These two triads, composed of six of the most important diagnostic scales, would be more than adequate to reflect any real changes in personality structure as a function of the administration of Stelazine to chronic psychotics.

When differences were obtained between pre- and post-treatment scores

on the vocabulary and abstract reasoning tests of the Shipley-Hartford Intelligence Scale, the non-significant result obtained by the analysis of these difference scores probably occurred as a function of a possible suppression effect on higher neural centers on the Central Nervous System.

Stelazine apparently has a cumulative effect upon human functioning and behavior. This may be an adequate explanation for the difference in statistical results obtained by the drug treated patients on Hospital Adjustment Scale scores when pre-treatment test results were compared with those obtained after 21 days of drug treatment and with those obtained after 66 days of drug treatment. A cumulative effect of the drug would account for the obtained statistical significance ($p < .05$) in the second comparison as well as the lack of significance found in the first comparison. These results suggest that another study of the psychological effects of Stelazine, conducted in a similar manner but free of the confounding effects of extraneous medication, might possibly find that the other three test instruments used in this study would obtain statistical significance in favor of Stelazine treated patients.

It was felt that several demonstrations of aggressive behavior by patients who became disturbed were the results of the energizing effects of Stelazine. After the identity of the experimental and control patients was made known, it was apparent that this hypothesis was incorrect. Only four aggressive demonstrations were observed in two patients in the drug treated group, but 11 explosive acts were listed for eight subjects in the placebo group. This fact supplies further evidence that Stelazine has tranquilizing effects as well as stimulating effects.

Bowen (3) reported that Stelazine is the most potent phenothiazine

derivative yet developed, and that is is 10 times more active than chlorpromazine. This experimental evidence leaves little room for doubt that Stelazine is a tranquilizer. Chlorpromazine apparently inhibits the chemoreceptors in the diencephalon, which seems to have an effect on many psychic and physiological processes integrated in the central and autonomic nervous systems. Griffiths' (7) hypothesis that similar effects occur when Stelazine is administered to rats, seems plausible. Apparently Stelazine activates the motor areas of the central nervous system, yet has an inhibiting effect on higher neural centers. This seems adequate to account for the obtained results of the four psychological tests administered to measure the effects of Stelazine in the present study.

CHAPTER VI

SUMMARY AND CONCLUSIONS

The psychological effects of Stelazine on chronic psychotic hospital patients were studied for a period of 66 days by using two matched groups of subjects; one treated with the drug and the other treated with a placebo. All subjects in both treatment groups were rated on the Hospital Adjustment Scale (HAS) and the Malamud-Sands Psychiatric Rating Scale prior to treatment, after 21 days of treatment, and after 66 days of treatment. The Minnesota Multiphasic Personality Inventory (MMPI) and the Shipley-Hartford Intelligence Scale were administered prior to treatment and after 66 days of treatment.

Results of the HAS scores indicated that the drug treated subjects improved significantly in their adjustments to hospital living conditions when treated with Stelazine for the 66 days duration of the study ($p < .05$). Improvements in drug patients approached significance after 21 days of Stelazine treatment. When HAS scores for the drug and placebo treated patients were compared, a significant improvement was observed in favor of the drug treated group ($p < .05$).

The Malamud-Sands Psychiatric Rating Scale did not reflect significant behavioral differences between drug and placebo treated patients; however, this scale proved to be a valid instrument in the detection of the energizing effects of Stelazine. Scores between prior to treatment and following treatment differences in performance on the MMPI and Shipley-Hartford Intelligence Scale for both treatment groups did not

provide statistically significant results between changes in behavior on either test for either treatment group.

On the basis of psychological data made available in the present study, the following conclusions seem warranted:

1. The only response measure used with sufficient sensitivity to detect beneficial behavioral effects of Stelazine treatment was the Hospital Adjustment Scale.
2. It is suggested that a similar study, using a larger number of subjects, more uniform controls of medication, and possibly other response measures, would possibly provide more valid indications of the effectiveness of Stelazine as an agent for the treatment of chronic psychotic hospital patients.

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A P P E N D I X

APPENDIX A

APPENDIX TABLE I

EFFECTS OF STELAZINE ON HOSPITAL ADJUSTMENT SCALE SCORES

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	136.80	136.80	4.40	<.05
Error	28	870.35	31.08		
Trials	1	2.01	2.01	0.28	N.S.
Trials X Treatments	1	4.44	4.44	0.62	N.S.
Error	28	200.05	7.14		
Total	59	1213.65			

APPENDIX B

APPENDIX TABLE II

EFFECTS OF STELAZINE ON MALAMUD-SANDS PSYCHIATRIC RATING SCALE SCORES

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	35.42	35.42	1.03	N.S.
Error	28	961.33	34.33		
Trials	1	30.81	30.81	1.78	N.S.
Trials X Treatments	1	21.54	21.54	1.24	N.S.
Error	28	484.15	17.29		
Total	59	1533.25			

APPENDIX C

APPENDIX TABLE III

ANALYSIS OF VARIANCE OF DIFFERENCES BETWEEN PRE- AND POST-TREATMENT NEUROTIC TRIAD SCORES ON THE MMPI

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	.2293	.2293	.019	N.S.
Error	28	339.8780	12.1385		
Total	29	340.1073			

APPENDIX TABLE IV

ANALYSIS OF VARIANCE OF DIFFERENCES BETWEEN PRE- AND POST-TREATMENT PSYCHOTIC TRIAD SCORES ON THE MMPI

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	.0448	.0448	.0007	N.S.
Error	28	1629.5577	58.1984		
Total	29	1629.6025			

APPENDIX D

APPENDIX TABLE V

ANALYSIS OF VARIANCE OF DIFFERENCES BETWEEN PRE- AND POST-TREATMENT VOCABULARY SCORES ON THE SHIPLEY-HARTFORD INTELLIGENCE SCALE

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	10.53	10.53	.87	N.S.
Error	28	336.94	12.03		
Total	29	347.47			

APPENDIX TABLE VI

ANALYSIS OF VARIANCE OF DIFFERENCES BETWEEN PRE- AND POST-TREATMENT ABSTRACT REASONING SCORES ON THE SHIPLEY-HARTFORD INTELLIGENCE SCALE

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	p
Treatments	1	1.16	1.16	.08	N.S.
Error	28	460.71	16.45		
Total	29	461.87			

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